

VOL. 108 • NO. 2804 • PAGES 313-324

September 24, 1959

Science



Elvin C. Stakman
President of the AAAS, 1959



There's Less "Spot Chasing"

WITH THE NEW L&N
Type E
GALVANOMETER

HIGH on the list of conveniences which the Type E offers to users of sensitive galvanometers is freedom from frequent "spot chasing."

In addition to the large, primary light spot which travels along the 100 mm scale with full galvanometer sensitivity, there is a smaller, brighter secondary spot.

Because a given voltage moves the secondary spot only one-tenth as far as the primary, the effective length of the scale is increased to 1000 mm. So you actually get an approximate reading of any deflection which would appear on a full meter scale with a conventional lamp and scale galvanometer.

Probably even more important is the fact that the secondary spot is so bright and moves so slowly—one-tenth as fast as the primary—that when it does shoot off the scale you usually see it go. You know immediately in which direction

you must correct to bring the circuit to the balance point. You seldom lose both spots so completely that you have to chase in both directions to discover the unbalance.

For further information, write to Leeds & Northrup Co., 4926 Stenton Ave., Phila. 44, Pa.

CHARACTERISTICS

List No.	Sensitivity per mm scale division	Nominal Period, Seconds	Nominal Resistance, Ohms		
			External	Critical	System
2430-a	0.5 mv	3	50		17
2430-c	0.005 ma	2.5	400		25
2430-d	0.0005 ma	3	25,000		550



AMINO ACIDS

for Research

Amino acids, the nitrogenous components of proteins, are of vital importance to adequate growth, maintenance and repair of tissue. As a service to nutritional research, GBI offers the following products in convenient-sized packages at an economical price:

DL-alpha alanine	DL-leucine
Beta alanine	L-leucine
L-asparagine	L-lysine monohydrochloride
DL-aspartic acid	DL-methionine
L-arginine monohydrochloride	DL-norleucine
L-cystine	DL-ornithine
L-cysteine hydrochloride	DL-phenylalanine
L-glutamic acid	L-proline
Glutamine	DL-serine
Glycine	DL-threonine
L-histidine monohydrochloride	L-tryptophane
DL-homocystine	DL-tryptophane
Hydroxy-L-proline	L-tyrosine
DL-isoleucine	DL-valine

Write for our Descriptive Price List for complete information on diet materials, crystalline vitamins, microbiological media and miscellaneous biochemicals for research.

GENERAL BIOCHEMICALS, INC.

60 LABORATORY PARK

CHAGRIN FALLS, OHIO



Science

Mildred Atwood

F. A. Moulton

Acting Editor

Advertising Manager

Publications Committee

Farrington Daniels, John E. Flynn, Kirtley F. Mather, Walter R. Miles, Malcolm H. Soule, Steven M. Spencer

Vol. 108 No. 2804 Friday, September 24, 1948

CONTENTS

Address of the President of the United States 313

The One World of Stars: *Harlow Shapley* 315

News and Notes 322

Technical Papers

The Quantitative Theory of Autoradiography Illustrated Through Experiments With P^{32} in the Chick Embryo: *Herman Branson and Louis A. Hansborough* 327

Crystalline Serotonin: *Maurice M. Rapport, Arda Alden Green, and Irvine H. Page* 329

The Action of Ryanodine on the Contractile Process in Striated Muscle: *G. A. Edwards, et al.* 330

The Homing Tendency of Shad: *Edgar H. Hollis* 332

Effect of Antiserum and Prolonged Cultivation on the Agglutinative Characteristics of a Type I Meningocoecus: *Dorothy Neuhof Naiman* 334

The Inactivation of Invertase by Tyrosinase: *Irwin W. Sizer* 335

Mammary Carcinoma in Female Rats Fed 2-Acetylaminofluorene: *R. W. Engel and D. H. Copeland* 336

In the Laboratory

A Simple Micro-Beaker for Use With the Beckman pH Meter (Model G): *Victor H. Dietz* 338

A Rapid Method for Preparing DDT in the Laboratory: *Joseph M. Ginsburg* 339

Radioangiography: A New Method for Studying the Blood Flow Through the Chambers of the Heart in Human Beings: *Myron Prinzmetal, et al.* 340

Book Reviews

Principles of jet propulsion and gas turbines: *M. J. Zuerow*. Reviewed by *Howard S. Seifert* 342

Advances in military medicine: *C. Andrus, et al. (Eds.)*. Reviewed by *Morris C. Leikind* 342

(Cover photo by Science Service, Inc.)

Science, a weekly journal, is published each Friday by the American Association for the Advancement of Science at The Business Press, Incorporated, N. Queen St. and McGovern Ave., Lancaster, Pa. Founded in 1880, it has been since 1900 the official publication of the AAAS. Editorial and Advertising Offices, 1515 Massachusetts Avenue, N.W., Washington 5, D.C. Telephone, EXecutive 6060 or 6061. Cable address, SCIMAG, Washington, D.C. Entered as second-class matter at the Post Office at Lancaster, Pa., January 13, 1948, under the Act of March 3, 1879. Acceptance for mailing at the special rate postage provided for in the Act of February 28, 1925, embodied in paragraph 4, Sec. 538, P. L. and R., authorized January 13, 1948.

Articles offered for publication should be sent to the Editor. The AAAS assumes no responsibility for the opinions expressed by contributors. Membership correspondence for the AAAS should be sent to the Administrative Secretary.

Annual subscription, \$7.50; single copies, 25¢; foreign postage (outside the Pan-American Union), \$1.00 extra;

Canadian postage, 50¢ extra. Remittances and orders for subscription and single copies should be sent to the Circulation Department, AAAS, North Queen Street and McGovern Avenue, Lancaster, Pennsylvania, and 1515 Massachusetts Avenue, N.W., Washington 5, D.C. Claims for missing numbers will not be allowed if received more than 60 days from date of issue. No claims allowed from subscribers in Central Europe, Asia, or the Pacific Islands other than Hawaii or because of failure to notify the Circulation Department of a change of address or because copy is missing from the file.

Change of address. Four weeks notice is required for change of address. This should be sent to Science, 1515 Massachusetts Avenue, N.W., Washington 5, D.C. When ordering a change, please furnish an address stencil label from a recent issue. Address changes can be made only if the old as well as the new address is supplied.

The American Association for the Advancement of Science also publishes *The Scientific Monthly*. Subscription rates on request.

SCIENCE, September 24, 1948, Vol. 108

Address of the President of the United States*

I am deeply honored in being with you tonight on the 100th anniversary of the founding of the American Association for the Advancement of Science. As President of the United States, I welcome you to Washington.

In the 100 years since this Association was organized, science has helped transform the United States into the most productive nation in the world. I know that in your meetings this week you will be looking back over the progress of American science in the past century. I also know that you are much more interested in looking into the future.

You are looking forward, I know, because we stand at this moment at the threshold of revolutionary developments. Scientific research daily becomes more important to our agriculture, our industry, and our health. The members of this Association know better than I what developments to expect in the years ahead in physics, in chemistry, in biology and the other sciences, but I am certain of this—that science will change our lives in the century ahead even more than it has changed them in the 100 years just past.

I hope you will also be thinking about the relationship between science and our national policy.

Two years ago, I appointed a Scientific Research Board. Its report, entitled *Science and public policy*, was submitted last fall to the 80th Congress. That report stressed the importance of science to our national welfare, and it contained a number of important recommendations. The most important were these:

First, we should double our total public and private allocations of funds to the sciences. We are now devoting, through Federal and private expenditure, little more than \$1,000,000,000 for research and development per year. With a national income of more than \$200,000,000,000 annually, the Board felt that we should devote at least \$2,000,000,000 to scientific research and development each year.

Second, greater emphasis should be placed on basic research and on medical research.

Third, a National Science Foundation should be established.

Fourth, more aid should be granted to the universities, both for student scholarships and for research facilities.

Fifth, the work of the research agencies of the Federal Government should be better financed and coordinated.

I hope that you have been weighing these recommendations carefully and that, if you agree with me that they are sound, you will consider how they can be made effective national policies.

I know that you are also deeply concerned with the relationship of science to our national defense and security. Three years ago, when the fighting stopped, all of us were eager to return to our peacetime pursuits. The first thought of a great many of us was how to translate our wartime advances in scientific knowledge into better standards of living.

It is an unfortunate fact, however, that the peace we hoped for has not come quickly. We are still living in hazardous times. We are required to give unremitting thought to the defense of the United States at a period when defense has become incredibly more difficult. American scientists must like all the rest of our citizens, devote a part of their strength and skill to keeping the Nation strong. At a time when we hoped our scientific efforts could be directed almost exclusively to improving the well-being of our people, we must, instead, make unprecedented peacetime efforts to maintain our military strength. For we have learned—we have learned the hard and bitter way—that we cannot hope for lasting peace with justice if we do not remain strong in the cause of peace.

If we are to maintain the leadership in science that is essential to national strength, we must vigorously press ahead in research. There is one simple axiom on which this thought is based. The secrets of nature are not our monopoly. Any nation that is willing and able to make the effort can learn the secrets that we have learned. Such a nation may, indeed, discover new facts of nature we have not yet discovered.

Our problem, therefore, is not a static one of preserving what we have. Our problem is to continue to engage in pure—or fundamental—research in all scientific fields. Such research alone leads to striking developments that mean leadership. Yet it is precisely in this area that we, as a Nation, have been weakest. We have been strong in applied science and in technology, but in the past we have relied largely on Europe for basic knowledge.

Pure research is arduous, demanding, and difficult. It requires unusual intellectual powers. It requires extensive and specialized training. It requires intense concentration, possible only when all the faculties of the scientist are brought to bear on a problem, with no disturbances or distractions.

Some of the fundamental research necessary to our national interest is being undertaken by the Federal Government. The Government has, I believe, two obligations in connection with this research if we are to obtain the results we hope for. First, it must provide truly adequate funds and facilities; second, it must provide the working atmosphere in which research progress is possible.

* Delivered at the opening session of the Centennial Celebration of the AAAS, Monday evening, September 13, 1948.

As to the first point, the Government is developing impressive programs in many scientific fields. Fundamental research is being carried on for the National Military Establishment in the laboratories of the armed forces, of industry, and of our universities. The Atomic Energy Commission has been pushing its extensive research. The National Advisory Committee for Aeronautics has expanded its many aeronautical developments. The Federal Security Agency has engaged in extensive medical studies, in its own laboratories, like the National Institute of Health, and through grants to colleges and universities. Other Federal agencies, such as the Departments of Commerce, of Agriculture, and of the Interior, have pursued vigorous programs. The Inter-Departmental Committee on Scientific Research and Development, appointed by me last March, aids in coordinating the Government's many research programs. I sincerely hope that these programs will be further developed and coordinated by the early passage of a National Science Foundation bill.

The second obligation of the Federal Government in connection with basic research is to provide working conditions under which scientists will be encouraged to work for the Government. Scientists do not want to work in ivory towers, but they do want to work in an atmosphere free from suspicion, personal insult, or politically motivated attacks. It is highly unfortunate that we have not been able to maintain the proper conditions for best scientific work. This failure has grave implications for our national security and welfare.

There are some politicians who are under the impression that scientific knowledge belongs only to them. They seem to feel that it is dangerous to let scientists know anything about scientific developments in this country. This situation has been of increasing concern to me. It was highlighted by a telegram I received last week from 8 distinguished scientists. These men expressed their alarm at the deterioration of relations between scientists and the Government because of the frequent attacks which have been made on scientists in the ostensible name of security. The telegram points out that the actions of certain groups are "creating an atmosphere that makes men shun Government work," and that the Federal Government is losing the services of excellent scientists because they have been looked upon from certain quarters as "men not to be trusted." The telegram points out that scientists fully appreciate the need for sensible security measures. But scientists very understandably are reluctant to work where they are subject "to the possibility of smears that may ruin them professionally for life." That telegram was a balanced and sober presentation of a vital problem that concerns every American.

Continuous research by our best scientists is the key to American scientific leadership and true national security. This indispensable work may be made im-

possible by the creation of an atmosphere in which no man feels safe against the public airing of unfounded rumors, gossip, and vilification. Such an atmosphere is un-American. It is the climate of a totalitarian country in which scientists are expected to change their theories to match changes in the police state's propaganda line.

I hardly need remind this Association that it is primarily to scientists that we owe the existence of our atomic energy enterprise. It was the scientists who first saw the possibility of an atomic bomb. It was the scientists who proved the possibility. It was the scientists who first saw the need of security measures and who, on their own initiative, clamped down a tight lid of secrecy on all experiments. It must not be forgotten for a moment, and certainly it must not be obscured by any smear campaign, that but for the scientists we would have no atomic energy program.

We are only in the beginnings of the atomic age. The knowledge that we now have is but a fraction of the knowledge we must get, whether for peaceful uses or for national defense. We must depend on intensive research to acquire the further knowledge we need. We cannot drive scientists into our laboratories, but, if we tolerate reckless or unfair attacks we can certainly drive them out.

These are truths that every scientist knows. They are truths that the American people need to understand.

Science has no political affiliation. Concern for our national security is nonpartisan. Sober recognition of scientific research as the basis of our future national security should certainly be nonpartisan. All Americans have a solemn obligation to avoid those methods and procedures which are impeding scientific research—whether adopted mistakenly with good intent or advocated in the name of security by men with other axes to grind.

My emphasis tonight has been on the physical and biological sciences. These are obviously in the forefront in terms of our industry and technology. But the social sciences and related fields are at least as important in the present stage of human affairs. The physical sciences offer us tangible goods; the biological sciences, tangible cures. The social sciences offer us better ways of organizing our lives. I have high hopes, as our knowledge in these fields increases, that the social sciences will enable us to escape from those habits and thoughts which have resulted in so much strife and tragedy.

Now and in the years ahead, we need, more than anything else, the honest and uncompromising common sense of science. Science means a method of thought. That method is characterized by openmindedness, honesty, perseverance, and, above all, by an unflinching passion for knowledge and truth. When more of the peoples of the world have learned the ways of thought of the scientist, we shall have better reason to expect lasting peace and a fuller life for all.

The One World of Stars

Harlow Shapley

Harvard College Observatory

THE 6TH PRESIDENT OF THE UNITED STATES is accredited with the rather astonishing statement that one can judge the state of culture in a nation by the condition of its astronomical observatories. I trust that he meant that the better the astronomical situation, the higher the culture. It would be most distressing if he meant that when astronomers prosper, culture declines.

John Quincy Adams, who after persistent effort incited his Harvard College to undertake the first ambitious development of astronomical research in America, was succeeded in the White House by men whose devotion to culture did not include active promotion of national efforts to take care of the stars. Their interests were earthy, planetary in scope, or even merely continental. But the 32nd president (Franklin Roosevelt) took an important part in celebrating the quadricentennial of Copernicus, who was the father of modern sciences as well as the promulgator of the heliocentric theory of the solar system. Privately F.D.R. expressed whimsically a lack of sympathy for Copernicus—"He looked through the right end of the telescope, thus magnifying his problems. I use the wrong end of the telescope and it makes things much easier." Tonight the White House, through a distinguished representative, has again joined in a program involving stars and telescopes.

Stars and governments have long been associated. In ancient times the rulers made use of the charlatan astrologers to guide their acts and justify their sins. We now use professors in that role, and investment bankers. The Babylonian, Egyptian, Chaldean, Greek, and Roman cultures supported through their governments astronomical instrumentation and interpretation—sometimes with philosophers, sometimes with star-measuring devices.

But the modern association of government and astronomy is more significant. The great Royal Observatory in Greenwich was founded by Charles II; the Russian observatory in Pulkowa, which until its destruction in the recent World War held a dominant place in European astronomy, was founded by Czar Nicholas I; Germany's famous observatory at Potsdam was created at the request of the Crown Prince who became Kaiser Friedrich; the Vatican Observatory, located at the Pope's summer residence, is one of

Address of the retiring president, AAAS, delivered on the evening of September 13 in Constitution Hall, Washington, D. C., during the Association's Centennial Celebration.

the most important of the European astronomical institutions; President Avila Camacho personally subsidized and inaugurated the new astrophysical observatory at Tonanzintla, Puebla, where the largest telescope bears his name; and President John Quincy Adams took an outstanding part a century ago not only in the founding of the Harvard Observatory but in the dedication of the people's observatory at Cincinnati.

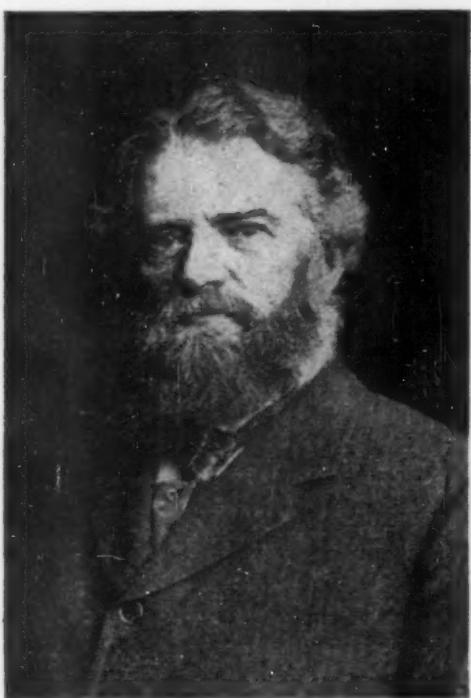
I cannot fully explain why heads of governments in these notable instances have been so keen on astronomical exploration—why they have been friendly and promotive of that most "useless" of human enterprises: only in small part, I would say, because of its association with navigation and almanacs; only in part because of the prestige of its erudite aloofness; and only in part because of the noncontroversial nature of celestial mechanics. Perhaps our primitive ancestors, who were not bothered by mazdas and neon and were therefore in closer contact with the stars, had accumulated over the centuries and millennia so much curiosity concerning those touchables that we continue to discharge the inherited responsibility of satisfying that curiosity about heavenly bodies. But these explanations are not complete. I remain surprised and also, quite naturally, pleased that astronomy, along with some of the other sciences, is able to maintain good international relations when economic, religious, and diplomatic intercourse is so very difficult.

In 1941, when American-Mexican relations were strained by the confiscation of oil-producing properties and also by polities and by the church-in-education policies below the Rio Grande, the government of Mexico invited 30 American astronomers to hold a convention in Mexico and participate in the inauguration of a new observatory. This astronomical gambit was followed in succeeding years by expeditions into Mexico (under Mexican government auspices and expense) of physicists, chemists, and mathematicians.

The first postwar technical scientific congress was held in 1946 by the Russian, Scandinavian, English, American, French, Vatican, Dutch, Belgian, and other astronomers. Was the conference permitted by suspicious governments because astronomers are harmless, or because they are convincingly devoted to non-nationalism in science? Nine Russian astronomers spent many months in America in 1947, visiting all the American observatories and taking part in conferences. Last month the USSR Academy of Sciences

invited the International Astronomical Union to hold its next worldwide conference in Leningrad—an invitation that was of course welcomed, because a score of Russian astronomers are on the International Astronomical Commissions and one of them is vice-president of our international scientific union. Eight Russians and several from Finland, Poland, Czechoslovakia, Austria, and Hungary attended this summer's meetings in Switzerland of astronomers from 30 countries. Apparently the sun, moon, and stars ride high above the nation-separating curtains.

To some extent also in meteorology, agriculture, geodesy, and special branches of medicine has the famous curtain been permeable during the past year or so. It is a net, which tangles operations somewhat, but with patience and persistence the obstructions set up by politicians and the agencies of statesmen are by-passed or overflowed, and the natural two-way traffic in goodwill and cooperation continues.



Simon Newcomb, the 24th president of the American Association for the Advancement of Science.

The "One World of Stars" is a reality, and its significance should not be ignored in other fields of science and art, and, in fact, one-worldness need not be confined to the cultural fields. The stars are supranational, as also are the laws of gravitation, genetics, radiation, nutrition. Cannot goodwill, human brotherhood, and a common ambition for the higher cultures also develop as boundary passers? Our series of evening lectures this week are aimed to illustrate for many fields the one-worldness of science. No more hopeful and constructive theme could be found to celebrate this 100th anniversary of our Association.

I shall proceed by discussing the internationalism of some major astronomical adventures and show that

international collaboration is essential for the progress of our science, and in these nervous days doubly important for the progress of international amity.

The 24th president of our Association for the Advancement of Science was Simon Newcomb. Somewhat incidentally he was a novelist, an economist, and a government official, but primarily he was a mathematical astronomer and one of the greatest of American scientists of the 19th Century. One of his early studies concerned the positions and motions of the sun, moon, and planets. He sought to bring order out of the chaos resulting from much uncoordinated measurement, in the many national observatories. Jupiter and Saturn are rather obstreperous in the way they push and pull around the smaller planets, ours included. But by using all the old and modern measures of their positions, Newcomb and his assistants, after cleaning the observations properly, could develop theories to predict accurately what would happen in the years to come.

It is definitely an international job—this refined study of planetary motions—and in 1871 we find Newcomb in Germany looking up the old records and then in France digging into the century-old archives for the observations made by gone and forgotten observers. At the Paris Observatory he worked diligently on the stars and planets that are the property of all nations and remained essentially oblivious to the cannonading which the French were then using to settle a political question.

Going further back, we recall that in 1780 the British military governor of the Penobscot Bay area gave permission to the representatives of the American Academy of Arts and Sciences and of Harvard University to go to the Maine coast for the observation of a total eclipse of the sun. Although the Americans and British were busy with the Revolutionary War, this astronomical enterprise seemed to be sufficiently worthy, and arrangements for the trip were easily made. The available maps, by the way, were faulty, and the observers missed the totality by locating at the south edge of the path. But the expedition was not a failure. In a nice demonstration of serendipity, the astronomers, through this accident, observed something more interesting than the solar corona which they journeyed to see. The Rev. Mr. Samuel Williams, the Harvard professor of natural philosophy, saw for the first time and described the brilliant beads of light which frequently appear just as an eclipse is beginning or ending its total phase. These bright flares are the result of sunlight pouring through the deep mountain valleys on the moon. The eclipse beads of Revolutionary War time were described again 50 years later by an Englishman and are now unfairly known by his name. They are Baily's beads, not Williams' beads.

as they should be in the name of justice. But astronomers are not inclined to make an international incident of the matter. They are not asking His Majesty's Government whom the devil they think they are pushing around.

In fact, astronomers and other scientists are not natural warmakers. The real fight is against unknowns, not against neighbors. Scientists' problems are world problems. The laws of physics and biology are universal. There is no place for selfish nationalism in astronomy or medicine, in mathematics or meteorology. What one scientist discovers is the property of the world of science and the world of all men.¹

There is another well-known illustration that science and man's interest in science transcend war hatreds and work to decrease national prejudices. During his great travels of scientific discovery in the late 18th Century, the famous English navigator, Capt. James Cook, was protected by order of the American government, through the agency of Benjamin Franklin, from the American privateers that roamed the ocean and harassed British shipping.

During our recent World War the astronomers kept up a sort of impersonal contact across or around the battle lines. I remember, for instance, that a Russian astronomer at his observatory south of the Caucasus on the Turkish frontier in Asia discovered a new comet. The German armies were overrunning western Russia, and terrible battles were in progress in the northern Caucasus. The discovery was radioed across the battle lines to Moscow, and Moscow found time and interest to radio it directly to the Harvard Observatory for further telegraphic distribution.

Also during the war, in Rumania, which was an ally of Germany at the time, a comet was discovered and reported to the Royal Astronomer in Bucharest, who reported it to the Royal Astronomer in Denmark, who transmitted it to the Chief Astronomer in Switzerland, who forwarded it to America. The U. S. Navy, by the way, checked up on this Rumanian comet rather carefully to see if it were subversive.

Not only in reporting astronomical events, but in prolonged researches, astronomers continue to demonstrate the One World of Stars. There is a striking recent story of cooperation that should be recorded,

¹ At least that is ideally true. In practice, in a society of free enterprise, many scientific discoveries in physics and chemistry are not at all free to all men. The discoveries become trade secrets and are developed for private profit, and only eventually for "all men." As business secrets, the discoveries and developments are not open to inspection by rivals in business, or by the United Nations. Our own American system of exploiting the fruits of science points to the difficulty of international inspection—for instance, in the search of atomic plots.

namely, the new and most accurate measurement of the distance from the earth to the sun—the solar parallax. This distance is the so-called "astronomical unit" of approximately 93,000,000 miles. It is a fundamental unit of measurement throughout the extraterrestrial universe. The ancient Greeks tried to estimate the distance and during the 18th and 19th Centuries much attention was given to the various ways, direct and indirect, of finding the solar parallax. The direct measures of the sun from this little planet of ours are clumsy; but since through gravitational principles all the distances between all the bodies in the solar system are linked together, it has been found best to operate indirectly and to measure the distance to the planets and deduce from them the solar distance. A small, rapidly moving planet has advantages, and therefore much attention has turned, since its discovery half a century ago, to the minor planet Eros, which is periodically brought, in its somewhat elongated orbit, very near to the earth. The sharpness of its image on the photographic plate permits a precision that is impossible in measuring objects of large angular diameter like the sun and moon. About 18 miles in diameter, this asteroid Eros is not ordinary. Most of the 1,500 tabulated minor planets stay on their reservation between the orbits of Mars and Jupiter. But Eros and a few other small ones follow comet-like orbits, and occasionally give astronomers the important opportunity of making highly precise measures of motion and position. These minor planets, although merely planetary fragments, accurately obey the planetary laws of motion and reveal, after much analysis, the distances separating earth and sun, moon and earth, and the other planetary separations. As a by-product, the analysis of the measures of Eros gives us a determination of the mass of the moon.

In 1931 Eros and terrestrial astronomers had one of their occasional near approaches—a separation of only 16,000,000 miles. We knew about it long in advance. In 1928 the astronomers of the world met in Holland, and plans were made in detail for the coming "opposition." Many observations should be made of many stars in many countries. Thirty-six observatories on 5 continents and Australia took part. No one explained the plan to the diplomats, no one even mentioned to them what was going on, because governments generally recognize that the planets are not controversial subjects. A special committee examined the possibilities and made assignments. From Australia to Canada, from Argentina to Sweden, from the Japanese Royal Observatory to the Harvard station on the Modder River near Bloemfontein, Orange Free State, we did our work at the appointed times.

The famous spectrum expert, Dr. Annie J. Cannon, of the Harvard Observatory, classified on a special series of photographs the spectra of the stars that would be used to compare with Eros as it hurried through the star fields. Where it would go we had roughly predicted, but, to improve the parallax of the sun, where it went must be known with the highest precision possible, and the colors of the stars deduced from Miss Cannon's spectrum classifications would have a bearing on the precision possible from micrometer settings. Eros is yellowish, and we would get into trouble with refraction and other difficulties if its position were derived from comparisons with deep red stars or those peculiarly blue.

After a few weeks in 1931 Eros went on about its business, becoming too faint and far away to interest astronomers further; but the thousands of measures remained. The prolonged labor of deducing the parallax lay ahead. The measures by international arrangement were sent to His Majesty's Astronomer at the Cape of Good Hope, who is now the Astronomer Royal of England, Sir Harold Spencer-Jones. To him had been assigned the heavy job of analysis.

The micrometric measures of Eros from 15 observatories entered the final determinations of the parallax. Leipzig, Greenwich, and Berlin took important observing assignments, completing the work before the British-German interchange consisted only of murderous bombs and propaganda. Finally, in 1941, at the height of the world's worst war, in which maddened, frightened nations were trying at great expense of human life and wealth to destroy each other, the Astronomer Royal calmly announced that the best value of the solar distance, thanks to the international cooperation of scientists, is 93,005,000 miles, with an uncertainty of only 8,000 miles. The new value of the solar parallax was not greatly different from the values previously determined, but the uncertainty of the determination had been reduced to a twenty-fifth of the earlier uncertainty. The new value was, of course, immediately communicated to the scientists of all the warring nations. Human knowledge of a constant of Nature had gained through cooperative internationalism. Who gained, and what did they gain, by the concurrent bitter hates of nationalism and by the slaughters of a science-engulfing war? But war could not be avoided, we say. Perhaps the eccentricity of the orbit of Eros needs international cooperation less than the eccentricities of human behavior.

The one world of stars could be illustrated indefinitely. I choose a few modern incidents that introduce the newer techniques, or show the necessity of international collaboration.

The sun is an international power plant and plays no favorites. The solar astronomers the world over began active collaboration 40 years ago. They set up central bureaus for the recording of solar phenomena. Special observatories for the study of the sun have been established in India, California, northern Chile, France, Colorado, Michigan, Switzerland, Austria, Holland, Russia, and elsewhere. Some of the observations are reported daily through a telegraphic interchange, because certain phenomena associated with the sun operate swiftly, and they influence, in a significant fashion, the ionospheric layer of the earth's atmosphere.

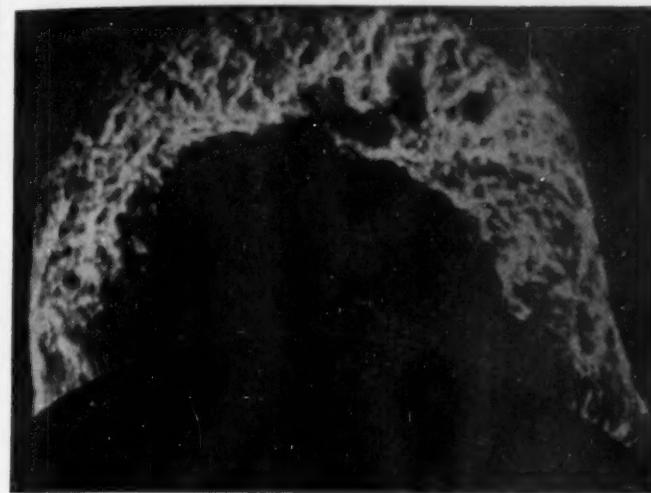
The sun brings together not only different countries but also the different sciences—it has shown steadily for 1,000,000,000 years and more. The problems of its radiation unite the botanist and the astronomer, the cosmologist and the physicist, the paleontologist and the weatherman. It has inspired the worship of primitive men, and its transformation of atoms of matter into the energy of radiation inspires the utmost in modern technology. The sun is indeed the guiding light to the atomic age.

But we know so little about the sun—its spots, its spicules, its prominences, and corona. To solve such mysteries, the combined efforts of all astrophysicists are needed. Let's start our exposition with the corona, that ethereal high solar atmosphere that was formerly seen only during the total eclipse of the sun. An ingenious young French astronomer, Bernard Lyot, less than 20 years ago began to solve the two-generation-old problem—how to see the elusive solar corona without the necessity of the rare solar eclipse. He installed his own eclipse-producing moon inside his telescope. He did it so carefully that the resulting coronagraph, when used on a high mountain above the earth's layer of dust—on Pic du Midi in southern France—brought out the faint glow of coronal light which is lost in the glare of sunlight unless the disc of the sun is carefully concealed by the moon or by a reasonable and effective facsimile thereof.

Following and modifying Lyot's technique, Menzel and Roberts, of the Harvard Observatory, built up and have been using for several years the only coronagraph of the Western Hemisphere. It is located high in the Rocky Mountains at Climax, Colorado, and is operated under the joint auspices of Harvard and the University of Colorado. It daily records the corona and its changing intensity, but it also records with proper accessory apparatus, the solar prominences. Those hot solar clouds, as recorded, for example, at the McMath-Hulbert Observatory of the University of Michigan, change form from hour to

hour, some explosively and some slowly. The coronagraph permits the making of continuous pictures—one exposure every half minute, for example. When these exposures are properly speeded up, we have a motion picture of the mighty gas storms on the surface of this nearby and typical star of ours.

The new photographs from the Climax station of the Harvard Observatory are selected to show various types of activity. Some are eruptive flashes, others long-continuing storms. The speeds of the motions are 3,000 to 4,000 times the speed of the winds in our own atmosphere. The photographic records are best made in the red light of the atom of hydrogen, but there are similar convulsions in the green, blue, and violet radiations of hydrogen and in the light emitted from other atoms of the solar atmosphere—for example, calcium and iron. The temperatures are



Solar prominence photographed in hydrogen light at the Climax, Colorado, station of the Harvard Observatory.

several thousands of degrees Centigrade. The pictures show that more of the motions are directed downward into the sun than upward from its surface. Why this strange tendency of more material coming down than going up? We do not fully know. The radiating material apparently is elevated to some thousands or tens of thousands of miles above the solar surface without emitting the red hydrogen light. Several mechanisms for this action have been suggested. More observations are needed, in finer detail.

It is of interest to record that the solar explosions are internationally studied—observationally and theoretically. American, French, Swedish, English, Australian, German, and now Austrian and Russian scientists are working on these problems, in part because of their basic scientific interest and in part because the radiations from the prominences and the overlying corona, and other solar radiations, operate at long distance on the earth's atmosphere, affecting the radio transmission, the Northern Lights, the

magnetic needle, and possibly to some extent the earth's weather. The solar corona is still something of a mystery, especially its astonishing temperature, which may be something like $1,000,000^{\circ}$ C, although the surface of the sun it surrounds has a temperature of only $6,000^{\circ}$.

The chemical composition of the material in the solar corona, for 60 years a mystery, appears, however, to be solved, and again the boundaries between nations were ignored. Following ideas and intimations provided by many spectroscopists, and especially following the work of Grotrian, German astrophysicist, Dr. B. Edlen, a young Swedish physicist, has come out with the astonishing theory that the scintillating airy corona of the sun owes its chief radiation to atoms of heavy elements. Before Grotrian and Edlen, scientists generally believed that the corona must be composed of very light elements; but now we find that the excited atoms of iron, nickel, and calcium provide most of the radiation. These atoms are highly ionized. Their outer electrons have been blown away by the excessive radiations, or whatever it is that excites and ionizes so violently these common heavy elements in the upper atmosphere of the sun.

We must learn more about this business, because what works on the sun doubtless works on the billions of stars of our Milky Way galaxy. And we shall learn more, if you keep us out of a civilization-ruining war, because the scientists of a dozen nations are turning their mathematical, observational, and interpretational skills to the question: How did that iron get into the rare upper solar atmosphere, and what is agitating it so excitedly that the excitement jets across 93,000,000 miles of space and disturbs our terrestrial radios?

The recent war, which we fought to preserve freedom and civilization, and doubtless for other reasons, did pretty badly by scientific civilization in many countries, especially interrupting the energetic and ambitious Japanese scientists. In a devastated and vanquished country, the surviving scientific laboratories and observatories are not prosperous. We record, however, one exception in Japan. Before the war there was in that country a kindly old gentleman who was recognized the whole world over as our leader in a certain phase of geodesy—in the highly organized international enterprise called "The Study of the Variation of Latitude." Dr. Hisashi Kimura was the chairman of an international commission involving geodesists of a dozen nations. To this commission had been assigned, by scientists and governments, the job of keeping track of the wandering of the poles of the earth. The true latitude of a place, of this hall for instance, is its angular distance from the equator, or 90° minus its distance from the North Pole.

It is a constant, of course, if the Pole stays put, but that is just what the North Pole does not do. For reasons that I shall not outline for you, because in part they are complicated and in part they are unknown, the Pole wanders erratically over an area about the size of this room. If you should sometime go to the North Pole and want to place a flag or carve your initials, you should make your observations of position and act quickly, or the Pole will be elsewhere.

Of course we do not need to go to the Pole to study these wanderings. We can set up an observatory almost anywhere and, with observations of a special sort, on stars in or near the zenith, check up on the unsteadiness. To do it right, however, several observatories are needed. The stations must be, for the best effect, in different longitudes and preferably all on the same latitude circle. Years ago a network of 5 observatories was set up, one each in Italy, southern Russia, and Japan, and two in the United States, one in California and one in Maryland. The observations should be continuous throughout the years. They were continued throughout the second World War, but with serious interruptions, except in Russia and Japan.

After the death of Dr. Kimura, an Italian took over the coordinating responsibilities, and the four united nations—united in geodesy, that is—now continue to trace the wanderings of the Pole, the variations of latitude, the internal and external changes in our earth that cause these irregularities and challenge the human intellect. Here again it is as though there were an international mind that wants to know about the intricacies of the physical world and, to attain its goal, hopes not to be bothered by national boundaries.

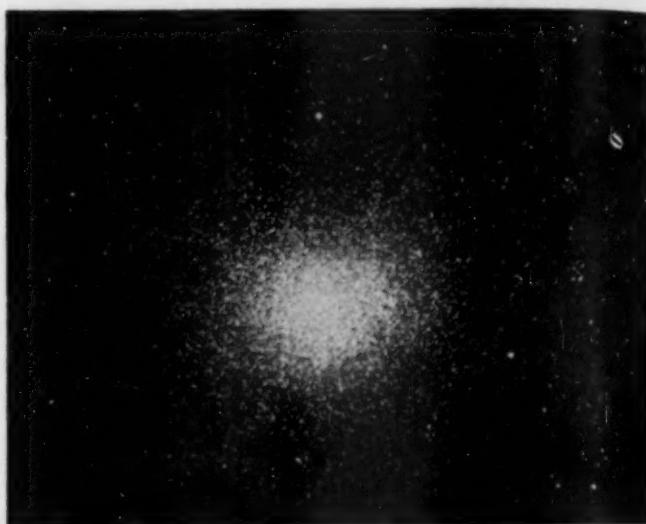
My story of the one world of stars goes all the way from the wobbles of the axis of a small planet that makes annual trips around one star to the total of all stars and the space-time in which they are involved. The relativity theory applies to the tiniest of units of energy and mass, and also to the galaxies at the outer bounds of the realm that is populated with galactic systems.

When Albert Einstein began to write his epoch-making theories, he was building directly on the mathematical explorations of Russian, German, Italian, Irish, and other mathematicians. The world-mind of mathematical physics was at work on the basic problems of the nature of the universe. National vanity, racial prestige, and stupid human strife were irrelevant.

The famous relativity theory, it was soon learned, could best be verified by astronomical tests; and at the end of the first World War, while the generals and

diplomats wrangled, the British astronomers, under the guidance of Sir Arthur Eddington, went off on a hazardous eclipse expedition to test the accuracy of a German's prediction about the bending of light at the edge of the sun. The formidable equations of the relativistic cosmogonies were solved by the Russian, Friedman, the Belgian, Lemaître, and the Americans, Robertson and Tolman.

The most famous little equation in the world, $E = Mc^2$, developed out of Einstein's early work just at the time astronomers needed it to help account for the obviously long life of the sun. The paleobotanical records, coupled with geochemistry, indicated that the sun had been pouring energy into the plant leaves for 1,000,000,000, years or more. That gave us a serious puzzle—the source of so much long-enduring solar radiation—but it was resolved by nuclear physics. To energize the plants and us, the stars feed on



The giant globular star cluster, Omega Centauri.

themselves. Their matter gradually melts into radiation. Atomic energy is released in the sun at just the right rate, through the building of hydrogen into helium. Thus it has been for a few billion years, and so it will likely be for a few trillion years more.

Already, years ago the atomic age was budding. For the astronomers it was in full bloom many years before the splitting sensation of Uranium 235. Experiments and interpretations in the field of atomic energy were made by the scientists of a dozen nations at the beginning of the atomic scare about 10 years ago. The one world of atoms was demonstrated as clearly as the world unity of astronomy, of biology, and of chemical reactions.

We can now build and split atoms in our laboratory, but there is nothing we can do with the galaxies, those gigantic wheel-shaped star systems, strewn by the millions throughout the recently discovered outer spaces. Nor can we do anything with those smaller sidereal systems, the beautiful globular clusters, except to study them and learn of their enormous

populations of giant stars, measure their times, energies, positions, and motions, guess at their origins and destinies, and bring back to the philosophies and religions of men the raw materials useful for the reorientation of man and his works in the new world of knowledge and intellectual opportunity.



A spiral galaxy of the southern sky.

These great spiral galaxies are probably similar in form to the one in which we are located. Others are irregular, like the nearby clouds of Magellan, to which the Harvard Observatory has paid much attention for the past 50 years. Still other galaxies are spheroidal and symmetrical, looking much like super-giant globular clusters, which indeed they may be.

A month ago about 40 of us (from a dozen countries), who were particularly interested in the problems of galaxies, met in Zurich, Switzerland, to talk over the problems demanding further study. It was an international gathering. The goal was the solution of difficult problems. There was no jockeying for national prestige, no manipulating of small observatories, no struts about manifest destinies and national aspirations. It was an assembly of those representing a unified world curiosity, a unified desire to understand the universe, a united front in a special battle against our common enemy, ignorance.

In our conference we discovered that we needed additional observations to test the existing theories about the nature of space, time, and the expanding universe; and we needed more theory to interpret some of the newer surprise-observations that do not fit into the currently acceptable patterns. We want the 200-inch telescope, when ready, to tell us more

about the speed of recession of galaxies heretofore too remote for spectrum analysis; and we want the new Schmidt-type reflectors to increase observationally the stability of our census of the whole meta-galaxy, through searching out the millions of individual galaxies that are within reach.

From the new Baker-Schmidt telescope—the international enterprise of Eire, the United States of America, and North Ireland—we need more detailed information on the nucleus of our own galaxy. To be completed a year from now, this powerful new-type instrument will be mounted on Harvard Kopje in the Orange Free State, South Africa, and there it will be in a strategic location, with the hub of our wheel-shaped galaxy passing conveniently every day directly overhead. It should bring in answers to some of the pressing questions about the nature of our galaxy and of galaxies in general.

It is fitting that these basic researches on the nature of the physical world, for the enlightenment of all the human world, is to be accomplished with the aid of an internationally owned and operated instrument, the Eire-America-North Ireland reflector. The most valuable written document in the Harvard archives, it seems to me, is the agreement between the Dunsink Observatory of the government of Eire, the Armagh Observatory of the Archbishopric of North Ireland, and the Harvard Observatory. It is a simple statement, but its importance lies in the fact that it is jointly signed by the Catholic Bishop of Dublin and the Protestant Archbishop of Armagh, North Ireland—a document unique in history, I believe, and symbolic of the willingness and desire to cooperate across religious and political boundaries when led by the stars.

Here we have revealed, it may be, a prime function of science, and of our Association for the Advancement of Science as it enters its second century. Supranationalism and cooperation across national boundaries are so simple and effective in the sciences that we have a clear responsibility to lead the way into an era of peace and human progress without which our efforts for human knowledge and human comforts will have been in vain. Our species of man is now at one of its critical epochs. Does it survive the crisis, through the use of intelligence and the submersion of avarice, or does it join the fossil biological failures of the past, which, through inability to meet their crises, have long ceased to greet nightly the world of enduring stars?



NEWS and Notes

Roberts Rugh, associate professor of biology, New York University, has been granted a year's leave of absence to become associate professor of radiology at the College of Physicians and Surgeons, Columbia University, where he will work on a project on the biological effects of radiation. This work is under the direction of G. Failla and is supported by the AEC.

Henry C. Thomas, formerly associate professor of chemistry, Yale University, recently joined the staff of the Chemistry Department, Brookhaven National Laboratory.

Alfred Brauer, professor of zoology, University of Kentucky, is on a 6-month leave of absence at the Oak Ridge National Laboratory, where he plans to apply radiation techniques to problems of organization of insect eggs.

Raymond C. Truex, formerly associate professor of anatomy, College of Physicians and Surgeons, Columbia University, has assumed the duties of professor and head of the Division of Anatomy at Hahnemann Medical College and Hospital in Philadelphia, and **Eleanor Yeakle**, formerly research associate in the Department of Pathology, Columbia University, has been appointed assistant professor of anatomy at Hahnemann.

George Matsuyama, who received his Ph.D. at Minnesota working with I. M. Kolthoff, has joined the chemistry staff at Wesleyan University with the rank of assistant professor. His research interests are in the field of polarography.

William W. Greulich, professor of anatomy at Stanford University, and Mrs. Greulich left September 15 by air for Japan to continue a study of the effect of atomic radiation on the growth and development of youthful victims of Hiroshima and Nagasaki atom bombs. The research project, started last year, is being conducted through a grant received by the NRC from the Atomic Energy Commission and is under the direction of the Council's Committee on Atomic Casualties. On this trip facilities of a new hospital-laboratory at Hiroshima will be available. The Greulichs are expected to return to Stanford in December.

Robert A. Cooley has recently resigned as supervisor of the Liquid Propellants Section of the Naval Ordnance Test Station, Inyokern, California, to accept a position as associate professor of physical chemistry at the University of Missouri School of Mines, Rolla.

Robert W. Boyle, director of the Division of Physics, National Research Council of Canada, will retire on October 2. From 1912 to 1929 he was professor and dean of applied sciences at the University of Alberta. In the latter year he organized the NRC division of which he has since been director. Dr. Boyle is well known for his work on ultrasonics.

John H. Lilly, formerly associate professor of zoology at the University of Wisconsin, has been named professor of zoology and entomology at Iowa State College, Ames.

Joseph W. Sausville, who has been associated with the Neapa Division, Fairchild Engine and Airplane Corporation, Oak Ridge, Tennessee, and **Howard E. Everson**, formerly of Western Reserve University, have been appointed assistant professors of chemistry at the University of Cincinnati.

John F. Cornman, assistant professor of ornamental horticulture at Cornell University, has been named first director of the Cornell Plantations, a unique combination of bo-

tanical gardens and arboreta which has been under development since the opening of Cornell in 1868. The 1,000-acre tract, in addition to garden and arboretum areas, includes a herbarium in the College of Agriculture, extensive laboratory and library facilities, and the collection of palms and cultivated plants in the Bailey Hortorium.

Alexander N. Winchell has accepted an appointment as visiting professor in the School of Geology of the University of Virginia for the present school year. He will continue to do some consulting work. His address until next June will be University Station, Charlottesville, Virginia.

Clinton N. Woolsey, associate professor of physiology and neurophysiology at the Johns Hopkins School of Medicine, has been appointed to the recently created Slichter research professorship of physiology at the Wisconsin Medical School. He will continue his studies in the field of neurophysiology, to which his scientific contributions have already been extensive. Dr. Woolsey becomes the first appointee to this Chair, established by the Wisconsin Alumni Research Foundation as the Charles Sumner Slichter professorship in the natural sciences in memory of the late Prof. Slichter.

E. W. Brandes has relinquished his responsibilities as head of the Division of Rubber Plant Investigations at the Plant Industry Station (USDA), Beltsville, Maryland, to give full time to the Division of Sugar Plant Investigations at the same Station. Dr. Brandes, long head of sugar research in the Bureau, since 1940 has served as head of both Divisions. **Robert D. Rands**, principal pathologist in charge of the cooperative Latin-American rubber development project, has succeeded Dr. Brandes as head of the Rubber Division, which since 1947 has continued research phases of the wartime domestic rubber-production projects in the Southwest.

L. R. Hafstad, director of the Institute for Cooperative Research of The Johns Hopkins University, will continue this year as executive secretary of the Research and Development Board, on leave from the University. **Arthur E. Ruark** is assistant director of the Institute, with offices in Baltimore, and also a member of the Technical Staff of the director's office, Applied Physics Laboratory, Silver Spring, Maryland.

Visitors to U. S.

Douglas A. Hartree, professor of mathematical physics at Cambridge University, will discuss calculating instruments and machines and their applications in a lecture series to be held at the University of Illinois September 27-October 1. Dr. Hartree's visit is being sponsored by the University Graduate College and a special computer committee of the University Research Board.

Carl Robinow, formerly on the staff of St. Bartholomew's Hospital in London and authority on the structure of bacteria, who came to the United States last December as a visiting professor at Indiana University, will be Walker-Ames professor of microbiology at the University of Washington during the fall quarter. In addition to his teaching duties at the University Dr. Robinow will continue his research work and also present several public lectures.

Grants and Awards

Hornell Hart, Duke University sociology professor, has been named winner of the Edward L. Bernays Atomic Energy Award. The Award, a \$1,000 government bond, was presented to Dr. Hart during the recent convention of the American Psychological Association in Boston. Dr. Hart's essay, "Social Science and the Atomic Crisis," submitted in a nationwide contest among leading social scientists sponsored by the Society for the Psychological Study of Social Issues, was judged the best action-related research in the social implications of atomic energy.

Nominations are being solicited for three \$1,000 awards to be presented by the American Institute of Nutrition at its annual meeting next spring. One of these, the award established by Mead Johnson and Company to promote researches dealing with the B-complex vitamins, will be given to the laboratory (nonclinical) or clinical research worker in the United States or Canada who, in the opinion of the judges, has published during the previous calendar year the most meritorious scientific report dealing with this field. It may, however, be recommended that the award be made to a worker for valuable contributions over an extended period of time. The award of \$1,000 and a gold medal made available by the Borden Company Foundation, Inc., will be in recognition of distinctive research by U. S. or Canadian investigators which has emphasized the nutritive significance of the components of milk or of dairy products. Although made primarily for publication of specific papers, this award may also be given for important contributions over an extended period of time and may be divided between two or more investigators. The Osborne and Mendel award, established by the Nutrition Foundation, Inc., for recognition of outstanding accomplishments in the general field of exploratory research in the science of nutrition, will be made to the investigator who, in the opinion of the judges, has made the most significant published contribution in the year preceding the Institute's annual meeting or who has published a series of contemporary papers of outstanding significance. This is open also to investigators in other countries, especially those sojourning in the United States or Canada for a period of time.

Nominations for these awards, accompanied by data relative to the accomplishments of the nominee, should be sent to the chairman of the Nominating Committee in each case before January 15, 1949. These chairmen are: B-complex award, Harold H. Williams, Cornell University, Ithaca, New York; Borden award, James M. Orten, Wayne University College of Medicine, Detroit 26, Michigan; Osborne and Mendel award, D. W. ago, has already produced electrons of

Woolley, Rockefeller Institute for Medical Research, New York City.

Colleges and Universities

The Stone Laboratory of Ohio State University, according to its director, Thomas H. Langlois, is continuing its probe, begun in 1938, of the prehistoric past of Lake Erie. The project, financed by the U. S. Geological Survey through the Great Lakes Research Institute, has its base of operations at the University laboratory located on Gibraltar Island. Here, the research group working under Ira T. Wilson, professor of biology at Heidelberg College, is attempting to determine how long the Lake Erie area was covered by glacier formations. Examinations are made of samples or "cores" of the sediment at various levels on the lake bottom. Exploration of the lake bottom to a depth 70 feet below its surface has now been made. Recent tests have shown that the upper 5 or 6 feet of bottom was composed of soft materials such as would be deposited by water of the present lake temperature. Below that depth, however, the cores brought to the surface were of a "varved" structure or series of layers of harder materials, indicating deposits in much colder water, such as that of a melting glacier.

Stanford University physicists, working under William W. Hansen, director of the Microwave Laboratory and co-inventor of the Klystron, are undertaking the production of an electron linear accelerator. The instrument, a gigantic atom smasher, is capable of hurling particles with 1,000,000,000 electron volts of energy. The project, sponsored by the Office of Naval Research, will extend over a three-year period.

Dr. Hansen predicts that the 160-foot accelerator will develop at least three times as much energy as the massive cyclotron at UCLA. The 400,000,000-electron volt output of this cyclotron is the greatest amount of energy that man has so far imparted to an atomic particle. A 12-foot "pilot model" of the accelerator, constructed by Dr. Hansen over a year ago, has already produced electrons of

6,000,000 electron volts. Through use of the new accelerator, Dr. Hansen hopes that experiments upon the fundamental nature of matter, creation of cosmic rays, protons, and neutrons may be made.

Reed College, Portland, Oregon, has announced 5 new staff appointments as follows: William L. Parker, Brooklyn Polytechnic Institute, as professor of physics; Kenneth E. Davis, University of Rochester, and Leo Seren, University of Idaho, as assistant professors of physics; Arthur H. Livermore, Cornell University Medical College, as assistant professor of chemistry; and George A. Livingston, UCLA, as botany instructor in the Biology Department.

Dr. Parker succeeds A. A. Knowlton, retiring head of the Reed Physics Department, who will serve as interim head of the Bennington College Physics Department. Raymond T. Ellickson, former associate professor of physics at Reed, has accepted the position of professor of physics and associate dean of the Graduate School, University of Oregon.

The Woman's Medical College of Pennsylvania recently established a Department of Oncology under a grant from the National Advisory Cancer Council. Isabella H. Perry will serve as director, with Mildred Pfeiffer acting as assistant director. The new program will include weekly general tumor conferences where a tumor board, representing the various departments and specialties, will confer on the problems presented by the cases referred to the conference; a tumor diagnostic clinic; and a monthly cancer research seminar.

The Division of Cancer Control, Department of Health, Commonwealth of Pennsylvania, has granted three fellowships in oncology to Cornealia Motley, Mary B. Dratman, and Janet Hampton. Sophie Brenner is also working in the Department under a state grant.

Industrial Laboratories

The General Electric Research Laboratory has completed a new 50,000,000-volt betatron for production of high-energy X-rays. The betatron will be employed in a study of

high-energy radiation on living organisms, conducted by the Biology Department of Union College with the support of the AEC. The penetrating, effective rays of this machine are superior to those of lower-voltage betatrons, and it is hoped that qualified medical scientists will discover their value in cancer treatment. The compact new betatron, when mounted on trunnions, permits direction of the beam toward the patient at any desired angle. A second 50,000,000-volt machine is now under construction for the National Bureau of Standards.

The first American betatron was made by Donald W. Kerst, University of Illinois physicist. On leave from the University, Dr. Kerst aided G-E scientists in building the 20,000,000-volt equipment subsequently loaned to the University. Later, Ernest E. Charlton, head of the X-ray Section of the Laboratory, and his associate, W. F. Westendorp, constructed the 100,000,000-volt device, duplicates of which will aid in atomic studies at the Clinton National Laboratory and the University of Chicago.

Dr. Charlton credits Dr. Westendorp with the "biasing" technique resulting in the compactness of the new betatron. Basically, the betatron consists of a large electromagnet, at whose core, between circular pole faces, is a doughnut-shaped vacuum tube. Electrons, emitted from a hot filament within the tube, are circulated and constantly accelerated while the magnetic field increases. As the field reaches its maximum, the orbit of the whirling electrons is shifted, and they hit a tungsten target. This, in turn, generates a beam of high-voltage X-rays occurring 60 times per second. Dr. Westendorp's method involves special "bucking" coils carrying alternate and direct current. The effect of the biasing direct current is to shift the zero line of the cycle so that the electrons may be introduced earlier. They can then be accelerated over approximately a third of the entire cycle rather than a quarter. With more trips around the doughnut, the electrons acquire greater energy.

Lewis Warrington Chubb, director emeritus of the Westinghouse Research Laboratories, recently retired after a

43-year association with the Laboratories. The veteran scientist joined Westinghouse in 1905, helped found the Research Laboratories in 1916, and in 1920 was named head of all radio engineering activities. Dr. Chubb served as director of the Laboratories from 1930 until assuming his honorary emeritus post last March.

Recipient of nearly every major engineering and scientific honor, Dr. Chubb holds over 150 patents covering inventions in radio, electronics, jet propulsion, telephony, electrical equipment, radar, etc. In 1947 he was awarded the John Fritz Medal, one of the Nation's highest tributes to scientists and engineers.

Meetings and Elections

The U. S. National Commission on UNESCO meets at Boston on September 27-29. Both general and sectional meetings are scheduled. Chairman of the two section meetings on "Natural Sciences," which will feature a general discussion of UNESCO's program in the natural sciences to date and of the proposed program for 1949, will be Harlow Shapley, representative of the AAAS on the U. S. National Commission. The panels on Conservation of Natural Resources and on the Popularization of Science will present reports. Section meetings will also consider the following topics: The Engineering Sciences in UNESCO, Exchanges and UNESCO, and Science and the Maintenance of Peace.

In preparation for the Boston meeting the NRC Committee on UNESCO, of which Bart J. Bok, of Harvard University, is chairman, has issued a report entitled "The Natural Sciences in UNESCO" (September 1, 1948). This report, copies of which may be obtained upon request from the Committee, 2101 Constitution Avenue, Washington 25, D. C., summarizes the activities of the Natural Sciences Division of UNESCO and brings before the National Commission certain recommendations by the NRC Committee with regard to the natural sciences program of UNESCO.

Columbia-Presbyterian Medical Center recently sent 5 specialists abroad, in keeping with its policy of promoting the exchange of knowledge

and experience with medical men in foreign countries. Howard C. Taylor, Jr., director of obstetrics and gynecology of the Presbyterian Hospital and professor of obstetrics and gynecology on Columbia's Faculty of Medicine, has been visiting various German cities for clinical work. Edmund P. Fowler, Jr., director of the Otolaryngology Service of Presbyterian Hospital and Columbia professor of otolaryngology, flew to Oslo, Norway, and Stockholm, Sweden. Jerome P. Webster, attending surgeon at Presbyterian Hospital and professor of clinical surgery of Columbia's Faculty of Medicine, is in Shanghai, China, to conduct an 8-week course in plastic surgery, thereby inaugurating a program to develop the teaching of plastic surgery in China; Dr. Webster will also lecture in Peking, Canton, and Nanking. Michael Heidelberger, chemist of the Presbyterian Hospital and professor of biochemistry at Columbia, planned to attend the 8th Congress of Biological Chemistry in Paris, and also to lecture on biochemistry and allied subjects in various French and Swiss cities. Henry T. Randall, assistant resident in surgery at Presbyterian Hospital, has been visiting cancer research centers in London, Edinburgh, Stockholm, Paris, and elsewhere to report on the latest trends in cancer research and treatment in those centers.

The 41st annual New England Intercollegiate Field Geologists Excursion is scheduled for October 9-10 at Burlington, Vermont. Charles G. Doll, professor of geology at the University of Vermont, will be host leader. Prof. Doll will be assisted on the hard rock, glacial, and economic geology trips by Marland P. Billings, Donald Chapman, Al Chidester, and others. Those planning to attend should make reservations at Hotel Vermont or Hotel Van Ness, Burlington.

The meeting of the International Cancer Research Commission, which was to have been held in Paris October 17-22, has been postponed until next year.

The 6th Annual Pittsburgh Conference on X-Ray and Electron Diffraction will be held November 19-20 at Carnegie Institute of Technology, nich,

Pittsburgh, Pennsylvania. This year's conference is being sponsored by the local members of the American Society for X-Ray and Electron Diffraction (ASXRED), Carnegie Institute of Technology, the University of Pittsburgh, and the Mellon Institute of Industrial Research.

Technical papers will be presented in four sessions on Friday and Saturday. The principal address of the Conference will be delivered Friday evening by Sir Lawrence Bragg, director, Cavendish Laboratory, Cambridge, England. Roman Smoluchowski, of the Metals Research Laboratory, Carnegie Institute, is serving as general chairman of the Conference, while Harold P. Klug, of the Mellon Institute, is acting as chairman of the Program Committee.

Those wishing to attend should send the necessary advance registration notice to: C. W. Cline, Aluminum Research Laboratories, Box 772, New Kensington, Pennsylvania.

The 30th summer meeting of the Mathematical Association of America was held at the University of Wisconsin, Madison, September 6-7, in conjunction with the summer meeting and colloquium of the American Mathematical Society and meetings of the Institute of Mathematical Statistics, the Econometric Society, and Section A of the AAAS. About 717 persons were in attendance, including 322 members of the Association. The list of speakers was given in the July 30 issue of *Science* (p. 104). R. L. Moore, of the University of Texas, gave his retiring address as vice-president of the AAAS and chairman of Section A on the subject "Spirals."

Plans were laid for the annual meeting of the Association to be held on December 31 at Ohio State University, for a meeting next June at Rensselaer Polytechnic Institute in conjunction with the meeting of the American Society of Engineering Education, and for the 31st summer meeting to be held in September 1949 at the University of Colorado.

The annual meeting of the Mt. Desert Island Biological Laboratory was held in its Bowen Hall, August 12, at Salsbury Cove, Maine. The officers elected for 1949 are: Dwight E. Min-

president; Roy P. Forster, secretary; John Whitecomb, treasurer; J. Wendell Burger, director; Mrs. H. V. Neal, clerk. Homer W. Smith and Philip R. White were elected to the Executive Committee, and Mary Gardiner and Edward Smith were chosen as new Trustees.

According to Dr. Burger, 29 biologists and assistants actively conducted research at the Laboratory during the current season, particular emphasis being placed on renal physiology and on tissue culture, the latter under the supervision of Philip White. Modernization of the Laboratory during the last few years was reported upon at the meeting. A grant from the American Philosophical Society has permitted the purchase of basic apparatus for work in physiology, while another grant from the same Society forms the Ulric Dahlgren Memorial Fund, the annual income from which will be used for fellowships at the Laboratory. Several of the Laboratory's 14 buildings have been given official names, thereby honoring distinguished zoologists and friends. These include: Bowen Hall, Byrnes Cottage, Dahlgren Hall, Halsey Laboratory, and Neal Laboratory.

The Chicago Chapter of the American Institute of Chemists has elected the following officers for the coming year: Johan A. Bjorksten, chairman; Herman S. Bloch, vice-chairman; Mary Alexander, Universal Oil Products Company, secretary-treasurer; Charles L. Thomas, national councilor; and Bruce M. Bare, Archie B. Cramer, Gustav Egloff, and Clifford A. Hampsell, Chapter councilors.

Scientists in many fields will be interested to learn that the *Review of petroleum geology in 1947* is now available for distribution as Vol. 43, No. 3, of the *Quarterly* of the Colorado School of Mines. According to H. M. Crain, director of publications at the School, this is the sixth such annual review published in the *Quarterly* in cooperation with the American Association of Petroleum Geologists. The review has been prepared by F. M. Van Tuyl, W. S. Levings, and L. W. LeRoy, who have had the cooperation of J. H. Johnson, R. C. Holmer, and H. E. Stommel, of the faculty of

the Colorado School of Mines, as well as other leaders in the fields of geology, geophysics, and petroleum engineering both here and abroad. Covered are important events of the

year; advances in petroleum geology and allied subjects, including developments in the training of geologists and geophysicists and new maps and publications of general interest; aerial photographs; world exploration and development; production and reserves; trends in petroleum geology and geophysics; and the future of the petroleum industry. Of the 334 pages, 128 are devoted to a bibliography of some 3,500 listings.

The review may be obtained from the Department of Publications, Colorado School of Mines, Golden, at \$3.00 a copy postpaid.

The National Registry of Rare Chemicals, 35 West 33rd Street, Chicago 16, Illinois, is presently interested in obtaining the following "wanted" chemicals: titanium tetrafluoride, glyoxal sulfate, pyocyanin, phenol sulfatase, 4,7-diaminodiphenylene oxide, titanium dichloride, dichlorophosphorylfluoride, 4-chloromethylimidazole, L-tartaric acid, hypoxanthine deoxyribose phosphoric acid, cytosine deoxyriboside, thymine deoxyribose phosphoric acid, diglycylglycine, magnesium ferrite, hypaphorine, tert.-butyl thionitrite, borneol glucuronide, alloxazine adenine dinucleotide, isocoumarin, and 9,10-diphenylenephenanthrene.

Annual Reviews, Inc., nonprofit organization with headquarters at Stanford University, recently announced two additional forthcoming volumes for 1950. In addition to the *Annual Review of Psychology* and the *Annual Review of Physical Chemistry*, (see *Science*, July 30, p. 106), plans are under way for publishing an *Annual Review of Medicine* and an *Annual Review of Plant Physiology*. The editorial board of the new *Annual Review of Medicine* will consist of Windsor Cooper Cutting, of Stanford University, editor; Henry Wise Newman, Stanford, associate editor; and an editorial committee with the following membership: Alfred Blalock, of Johns Hopkins Hospital; J. S. L. Browne, of the Royal Victoria Hospi-

tal, Montreal; Allan M. Butler, of Harvard Medical School; Eaton M. MacKay, of the Scripps Metabolic Clinic; and Sidney C. Madden, of Emory University.

For the *Annual Review of Plant Physiology* the editorial board will consist of Daniel I. Arnon, of the University of California, editor, and an editorial committee consisting of David R. Goddard, of the University of Pennsylvania; Paul J. Kramer, of Duke University; A. E. Murneek, of the University of Missouri; Marion W. Parker, of the Bureau of Plant Industry, USDA; and Kenneth V. Thimann, of Harvard University.

Nine new White Dwarf stars have recently been discovered by Willem J. Luyten, chairman of the Department of Astronomy, University of Minnesota, and David MacLeish, of the Cordoba Observatory in Argentina. These stars are so dense that, if a cubic inch of them were brought down to earth, the matter would weigh anywhere from 1 to 1,000 tons. Of the 100 White Dwarfs now known, 61 have been found through the work done on the motions of stars at the University of Minnesota, with the active participation of the Steward Observatory, University of Arizona, and of the Cordoba Observatory. The first White Dwarf was discovered by the law of gravitation before it was actually seen with a telescope in 1862.

These stars, although dwarfs in every respect from size to amount of light shed, are very hot on their surfaces. They shine with a light much whiter than that of the sun and often become even blue in color. Their discovery and significance not only caused a minor revolution in astronomical and physical thinking, but forged another and very important link in the chain of events leading to the atomic bomb, according to Dr. Luyten.

The Smithsonian Institution, Washington, D. C., under its curator of physical anthropology, T. D. Stewart, is building up a collection of minutely accurate casts of skulls and other fossil bones of primitive man and his apelike precursors. Through this collection, it is hoped to build a complete record, accessible in one

location, of the development of the entire human race. This will obviate the necessity for traveling to the many scattered locations where these manoid relics are now located. Should the original relics chance to be damaged or destroyed, casts can readily be made from the Smithsonian collection. A notable example of this Dr. Stewart pointed out, was the recent disappearance of the skulls of China man, second oldest generally recognized member of the human race of which remains have been found. These skulls, located in Peiping early in the war, were apparently lost at sea while being transported to a place of supposed safety. As the Smithsonian has accurate casts of the China man skulls, a record of this particular stage in man's development has not perished.

Make Plans for—

American Institute of Electrical Engineers, October 5-7, Washington, D. C.

American Society of Photogrammetry, semiannual meeting, October 7-8, Franklin Institute, Philadelphia, Pennsylvania.

1948 National Industrial Chemical Conference and National Chemical Exposition, October 12-16, Chicago Coliseum, Chicago.

Electrochemical Society, fall meeting, October 13-16, Pennsylvania Hotel, New York City.

Industrial Minerals Division, American Institute of Mining and Metallurgical Engineers, October 14-16, Sheraton-Coronado Hotel, St. Louis, Missouri; October 15, Elks Club, Los Angeles, California.

5th Annual Seminar for the Study and Practice of Dental Medicine, October 17-21, Desert Inn, Palm Springs, California.

National Academy of Sciences, autumn meeting, November 15-17, University of California, Berkeley; special visits to Stanford University, November 18, and to Los Angeles area, November 19-21.

TECHNICAL PAPERS

The Quantitative Theory of Autoradiography Illustrated Through Experiments With P^{32} in the Chick Embryo

HERMAN BRANSON and LOUIS A. HANSBOROUGH¹

The Graduate School, Howard University

In the experiments on the effects of vitamins on phosphorus metabolism in the chick embryo, our laboratory has undertaken a study of the autoradiographic technique as an excellent means of determining the distribution of P^{32} between the embryo and blastoderm. The techniques and interpretations of our results based upon some simple principles of photographic sensitometry reveal that the procedure is capable of yielding quantitative results.

ceived 1.38 μc).² These injections were performed on the afternoon of March 5, 1948. The eggs were allowed to stand for 4 hrs and were then placed in the incubator. After 24 hrs, a group was removed. The yolk was floated into warm Ringer's solution. The embryo with a portion of the blastoderm was snipped clear. The layer was washed and placed in a watch glass of warm Ringer's, where it was perfused with Bouin's solution. Fixation in Bouin's was continued for 24 hrs. The embryos were washed in 70% alcohol with a little lithium carbonate added, after which they were stained in borax carmine, dehydrated in dioxane, and mounted in Clarite.

Strips of Agfa Triple S Pan film were placed over the mounted embryos. The slides with the film were wrapped in black paper and put into a light-tight box on March 22. The film was removed on April 5, approxi-

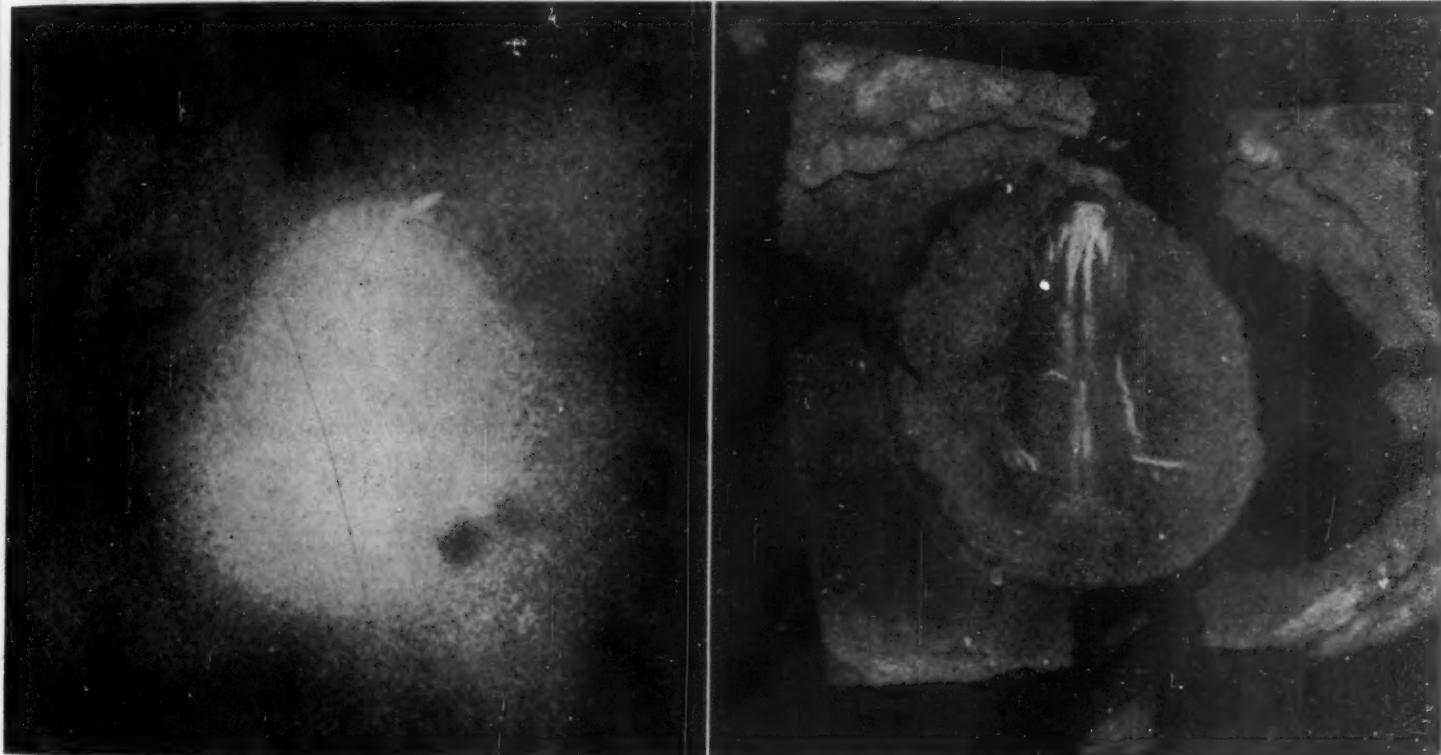


FIG. 1. The autoradiograph on the left is a mirror image of the 24-hr chick embryo on the right. Exposure was made through the glass coverslip of the mounted embryo. The dark spots on the lower right side of the autoradiograph are blemishes. The magnification in both photographs is approximately 10 \times .

Large brown New Hampshire eggs from the University of Maryland farm were sterilized on the blunt end with Lugol's solution and a small hole drilled through the shell without puncturing the outer shell membrane. A No. 27 needle on a tuberculin syringe was used to place 0.05 ml of NaH_2PO_4 in the egg white below the air chamber. The solution had an activity of 27.6 $\mu\text{c}/\text{ml}$ (i.e. each egg re-

¹ We are indebted to our colleagues for many suggestive discussions of this work. The program has been assisted by the Office of Naval Research.

mately 14.7 days later, and developed following standard procedure, to a gamma of one.

Good autoradiographs were obtained for all mounts—the 24-, 48-, and 72-hr embryos (see e.g. Fig. 1).

² These values were obtained by comparison with the Bureau of Standards reference sample of Radium D and E, No. 83. Our values on the intercomparison tests of I^{131} conducted by the National Bureau of Standards were consistently below the accepted value by approximately 43%. If the same ratio exists for our P^{32} measurements, the activity of the solution injected would be nearer 2.4 $\mu\text{c}/\text{egg}$.

There was a 17-day interval between the injection of the P^{32} solution and the beginning of the exposure. The equivalent activity which would have been in the whole egg at the beginning of the exposure (i.e. on March 22, assayed as 1.38 μ c on March 5) was 0.49 μ c/egg.

Although our initial concern has been with a procedure for obtaining autoradiographs with P^{32} in the chick embryo, the interpretation of our results leads directly to a simple quantitative theory which may have wider applicability in autoradiography with isotopes of not too long half-lives.

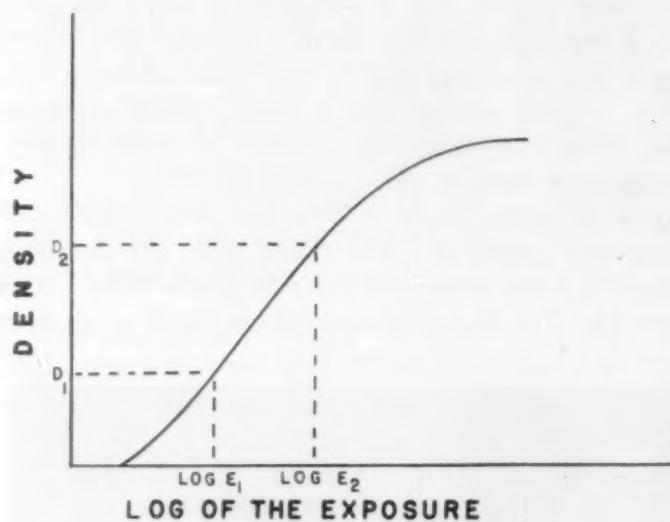


FIG. 2. An idealized Hurter and Driffield curve. The exposure is usually expressed in meter-candle-sec.

In photographic sensitometry, the Hurter and Driffield (H & D) characteristic curve expresses the relation between the density and the logarithm of the exposure. An idealized H & D curve is reproduced in Fig. 2. The slope of the linear portion is the gamma (γ) of the emulsion. This slope is not only a function of the emulsion but depends upon the developer, temperature, and time of development.

From two points on the linear portion of the H & D curve we have

$$(1) \quad \gamma = \frac{D_2 - D_1}{\log E_2 - \log E_1}.$$

In autoradiography, a reasonable definition of exposure is

$$dE \propto I_0 e^{-\lambda t} dt,$$

where I_0 is the initial activity of the radioactive substance in μ c or counts sec^{-1} and $e^{-\lambda t}$ is the decay factor for the radioactive isotope present in the sample. The formulation leads to

$$(2) \quad E = K I_0 \int_0^t e^{-\lambda t} dt = \frac{K I_0}{\lambda} (1 - e^{-\lambda t}) = E_{max} (1 - e^{-\lambda t}),$$

where t is the time the film is in contact with the radioactive material and K is a factor independent of time but dependent upon the geometry, the film characteristics, and the emanations from the radioactive substance. If I_0 is expressed in counts sec^{-1} , then for E to be in meter-candles-sec, K would have the units of (meter-candles-sec) counts $^{-1}$. Thus, K converts counts or disintegrations to the usual sensitometry unit.

Substituting the definition of E from equation (2) into equation (1) yields

$$\gamma = \frac{D_2 - D_1}{\log I_0 (2) - \log I_0 (1)},$$

where $I_0 (1)$ designates the initial intensity in the region marked (1) where the density is D_1 , with corresponding definitions for the other symbols. Thus, if the film is developed to a known γ and the density of two regions on the linear portion of the H & D curve measured, we would have the relative amounts of the radioactive isotope deposited in the two regions.

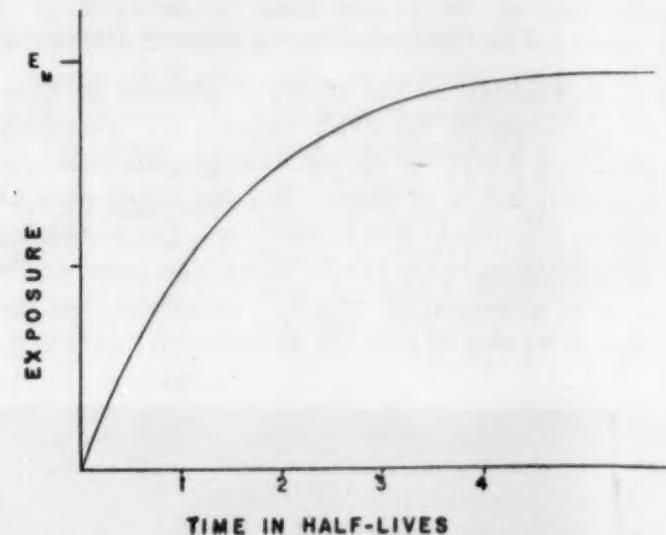


FIG. 3. A graph of the exposure as a function of half-life under the assumptions of this paper. E_m is the maximum exposure.

The graph of equation (2) in Fig. 3 is most instructive, for it relates the exposure to the time in contact. The most interesting point is that contact for a half-life results in an exposure equal to half that which would be received on indefinitely prolonged exposure. This is easily seen from equation (1), when

$$\begin{aligned} \gamma &= \frac{D_2 - D_1}{\log E_m - \log E_{m/2}} \\ &= \frac{D_2 - D_1}{\log 2}. \end{aligned}$$

Thus, a very long exposure would lead to a difference in density of only 0.3 γ .

In the autoradiograph of Fig. 1, the intense middle section of the embryo has a density D_2 , and the peripheral section, the region of the blastoderm, has a density D_1 . These densities were read on a Weston Photographic Analyzer, model 877, yielding $D_2 = 0.79$ and $D_1 = 0.33$. The background of the exposed film was taken at density zero. With these values, equation (1) gives

$$I_0 (2) = 3 I_0 (1).$$

That is, the region of the embryo has about three times as much radioactive phosphorus per unit area as the blastoderm. At this stage of development, the thicknesses of the two regions are comparable; hence we may conclude that the embryo is concentrating the available phosphorus at a fairly high rate.

Further experiments on direct film calibration with P^{32} are in progress in our laboratory.

Crystalline Serotonin¹

MAURICE M. RAPPORT, ARDA ALDEN GREEN,
and IRVINE H. PAGE

Research Division, Cleveland Clinic Foundation,
Cleveland, Ohio

Very few substances capable, at high dilution, of effecting changes in the caliber of blood vessels have been isolated from normal animal tissues. These are epinephrine, histamine, adenylic acid, acetylcholine, and choline. There are, however, several which, by their pharmacological actions, are known to be present although their identity has remained obscure. One of these is the vasoconstrictor which is present in serum and defibrinated blood and which appears in connection with platelet destruction and the clotting process.

Although the presence of the substance, as revealed by the ability of serum to cause vasoconstriction in organs through which it is perfused, has been recognized for almost 80 years, its physiological function is not yet clearly defined. The isolation of this substance may lead to clarification of its role as a hemostatic agent in intramuscular clotting and in cases, such as myocardial infarction following coronary thrombosis, where the prevention of spread of hemorrhage into tissues is important.

We are reporting the isolation of a crystalline substance from beef serum which may be responsible for the vasoconstrictor activity. The details of the partial purification involving the following five steps have already been reported (3): precipitation of serum proteins with ethyl alcohol; precipitation of inorganic salts, phosphatides, and amino acids with acetone; removal of chloroform-soluble impurities; extraction of the active principle with butyl alcohol from an aqueous solution saturated with ammonium sulfate; and precipitation of the active substance from the butyl alcohol with 5-nitrobarbituric acid. Isolation was attained with two additional steps. The 5-nitrobarbiturate complex was decomposed by the addition of acetone to its hot, saturated aqueous solution, and the precipitate was discarded. The filtrate was evaporated to dryness, and the residue was then extracted with warm absolute methanol. On cooling, this extract deposited clusters of prisms of the crude substance which, on recrystallization from water-acetone, formed thin, rhomboid, pale-yellow platelets (Fig. 1) melting at 207-212° (corr.) with decomposition (effervescence) on the Kofler micro hot-stage. The purest sample thus far obtained melted at 212-214° (corr.) with decomposition. The melting point behavior, despite the decomposition, closely parallels the degree of purity as determined by activity and colorimetric measurements.

The general behavior of the crystalline substance is suggestive of its homogeneity. We would like provisionally to name it *serotonin*, which indicates that its source is serum and its activity is one of causing constriction.

¹This investigation was partly supported by a grant from the Cardiovascular Study Section, U. S. Public Health Service.

Crystalline serotonin on sodium fusion gives positive tests for both nitrogen and sulfur and negative for halogen. The substance catalyzes the iodine-azide reaction of Feigl (1). A precipitate is obtained with barium

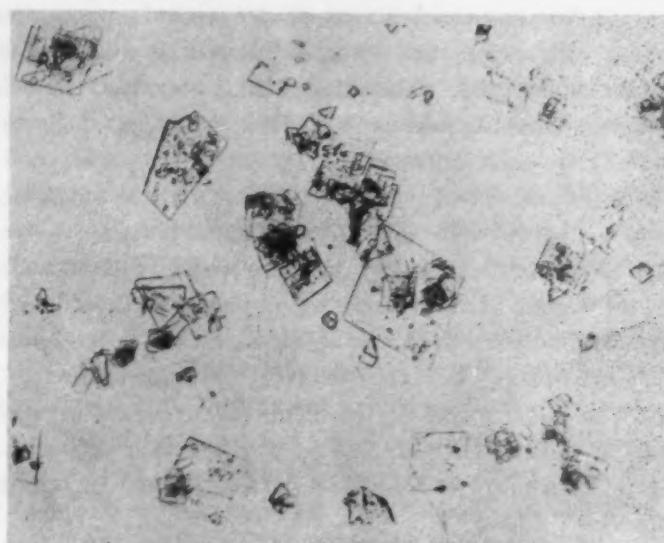


FIG. 1. Crystalline serotonin (x 125).

chloride, but not with silver nitrate. On the basis of this and other evidence, serotonin is believed to be a sulfate salt which may also contain organically bound sulfur. A single analysis (performed by E. Thommen, Basel) gave the following result: C, 41.4; H, 6.0; N, 17.0. These values are in good agreement with the ratios C₁₄: H₂₆: N₅ or C₁₇: H₃₀: N₆. The material responds in a

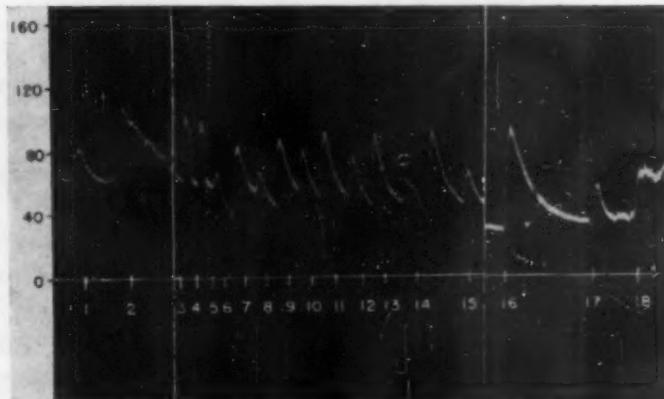


FIG. 2. Pressor effect of serotonin and adrenalin on intact, pithed, and tetraethyl ammonium-treated, anesthetized cat (No. 472); (1) adrenalin, 0.1 cc, 1/20,000; (2) serotonin, 0.1 cc, 1/4,000, pithed; (3-4) adrenalin; (5) serotonin; (6) adrenalin; (7) serotonin; (8) adrenalin; (9) serotonin; (10) adrenalin; (11) serotonin; (12) adrenalin; (13) tetraethyl ammonium, 5 mg/kg; (14) adrenalin; (15) serotonin, 4 more doses of 5 mg of tetraethyl ammonium; (16) adrenalin; (17) serotonin; (18) renin.

positive manner to well-established quantitative modifications of the Hopkins-Cole, Ehrlich, and Folin-Ciocalteu reactions.

The ultraviolet absorption spectrum in water at pH 5.4 has a maximum at 2,750 Å, K_{sp} (specific extinction coefficient) = 1.5×10^4 ; a shoulder with a point of inflection at 2,930 Å, K_{sp} = 1.2×10^4 ; and a minimum at 2,560 Å, K_{sp} = 1.0×10^4 .

Injected intravenously into dogs or cats anesthetized with pentobarbital, a solution of the crystalline material produced a rise in arterial pressure which was augmented in a sympathectomized animal (Fig. 2). In a few animals the response to small doses was depressor, becoming pressor after administration of tetraethyl ammonium chloride. The response after pithing was slightly reduced or unchanged. An isolated ring of rabbit's ileum was sharply contracted by injection of 17 μ g into the 30-ml Tyrode solution bath.

The vasoconstrictor activity of the crystalline substance in our assay method employing the perfused isolated rabbit ear preparation (2) is more than twice that of an equal weight of commercial epinephrine hydrochloride. Measurable constrictions are obtained by the injection of less than 0.002 μ g into the ear vessel preparation.

Work is in progress on the chemical structure of serotonin. A detailed description of the isolation procedure, together with more complete analytical data, will appear elsewhere.

References

1. FEIGL, F. *Qualitative analysis by spot tests.* (3rd ed.) New York: Elsevier, 1946. P. 353.
2. PAGE, I. H., and GREEN, A. A. In *Methods in medical research.* (Ed. by V. R. Potter.) Chicago: Year Book, 1948.
3. RAPPORT, M. M., GREEN, A. A., and PAGE, I. H. *J. biol. Chem.*, 1948, **174**, 735.

The Action of Ryanodine on the Contractile Process in Striated Muscle¹

G. A. EDWARDS, E. A. WEIANT, A. G. SLOCOMBE,
and K. D. ROEDER

Department of Biology, Tufts College

While it is unlikely that any chemical agent has a toxic action which is entirely tissue specific, there are many substances that act more rapidly or in lower concentrations in some tissues than in others. Such substances are of particular interest, since they may reveal differences in the enzymatic bases of specific tissue functions. A highly selective action of this kind is indicated by preliminary observations on the mode of action of derivatives of *Ryania speciosa*, which appear to affect specifically the contractile process in skeletal muscle.

Two derivatives of the tropical plant *Ryania speciosa* (Fam. Flacourtiaceae) known as L8A2—a crude extract soluble in alcohol but not in water, and the purified, water-soluble alkaloid, ryanodine—were obtained through the kindness of Dr. Ralph Heal, of Merck & Co., Inc. Experiments on intact animals and isolated nerve and muscle were performed to determine the site and mode of action of the toxic agent. The toxic symptoms observed in the

¹ The work described in this paper was done under contract between the Medical Division, Chemical Corps, U. S. Army, and Tufts College. Under the terms of this contract, the Chemical Corps neither restricts nor is responsible for the opinions or conclusions of the authors.

animals were similar for both the less active, crude extractives and the pure material.

The LD₅₀ has not been determined, but injection of 2–5 γ /gm produced symptoms in insects (*Periplaneta americana*, *Blaberus craniifer*, and *Platysamia cecropia*), frogs (*Rana pipiens*), and white mice. In the insects, injection of 0.05 ml of an insect saline solution containing 0.1 mg of ryanodine/ml has an entirely depressant effect. After 15 min the insect becomes generally sluggish, and in 25 min is unable to stand. At this point it appears to be partially paralyzed, being capable of making only slow, feeble movements of the appendages. It appears to be unresponsive to stimuli, and during the paralysis its legs can be placed in any position. Tremors and signs of central excitation are lacking, and feeble, slow reflexes may be elicited throughout the period of poisoning. From this dosage the insect remains partially paralyzed for about 48 hrs and then recovers. Higher doses kill, and lower doses produce a paralysis of lesser severity and shorter duration.

In the frog, injection of 5 γ /gm intraperitoneally results in complete rigor within 3 hrs. The first effect is flaccidity, occurring within an hour. Shortly thereafter the swallowing movements decrease in amplitude and frequency and eventually cease. Following this a pronounced rigor appears in the forelimbs and proceeds posteriorly.

The oxygen consumption of control and ryanodine-insect was determined in a modification of the Scholander volumetric microrespirometer (4). As found earlier in cockroaches by Chadwick and Hassett (1), and in the fiddler crab by Edwards (2), the flaccid paralysis of the cockroach (*Periplaneta*) was accompanied by a tremendous increase in oxygen consumption following injection of ryanodine in sublethal doses. With 0.05 ml of 10⁻⁵ ryanodine by weight O₂ consumption reached a peak of 9 times normal in 25 min, the time of onset of paralysis, and gradually decreased thereafter until a twice-normal level was attained in 3–4 hrs. This level of oxygen uptake was then maintained throughout the remaining 45 hr of paralysis. Injection of 0.05 ml of 10⁻⁵ ryanodine produced a peak oxygen uptake of 4.2 times normal within 50 min, the paralysis and increased oxygen consumption lasting 24 hrs. A peak of 2.3 times normal oxygen consumption was caused in 75 min by 0.05 ml of ryanodine 10⁻⁶. The paralysis and high rate of oxygen consumption lasted 8 hrs. Similar results were obtained with adults of *Blaberus*, diapausing pupae of *Platysamia cecropia*, and with isolated metathoracic legs of *Periplaneta*. In the cases where lethal doses of ryanodine were used, the oxygen consumption rose sharply at the onset of paralysis and then steadily decreased until death occurred. Actually, the only method of determining whether the insect was dead or paralyzed was to measure its oxygen consumption.

In an attempt to determine the site of action, oscillographic studies were made of the effect of the agent on electrical activity in irritable tissues of the cockroach by (a) applying a 10⁻⁴ solution directly to exposed ganglia and nerves and (b) studying the activity in ganglia and

erves of insects previously paralyzed by injection. Ryanodine 10^{-4} , a concentration approximately 50 times the concentration which would result if the effective dose were distributed evenly within the intact insect, failed to cause detectable changes in ganglionic or axonic transmission, spontaneous activity in the nerve cord, or sensory activity in the crural nerve. (For methods see ¹) Neuromuscular transmission, as indicated by the muscle action potential in the extensor tibiae muscle of the cockroach, also appeared to be unaffected by ryanodine. These results led to the conclusion that excitation and conduction in nerves, ganglia, and muscles are not affected by *Ryania* derivatives in the concentrations used, which leaves the contractile process in muscle as the only possible site at which *Ryania* extracts could act to produce the paralytic action.

TABLE 1

No. of legs used	Injected with:	No. of legs twitching			
		before injection	after 10 min	after 20 min	after 30 min
12	Saline	12	11	9	3
12	Ryanodine	12	0	0	0

This was confirmed by the observation that leg muscles of the roach failed to twitch on indirect or direct electrical stimulation 5–10 min after 10^{-4} ryanodine was perfused through the isolated metathoracic legs, whereas saline-perfused legs responded up to 30 min after preparation (see Table 1). A slow contracture was obtained in some of the poisoned legs with high rates of stimulation (100/sec at 10 v), though twitches to stimuli of 1–20/sec invariably disappeared both in amputated legs injected with ryanodine and in legs removed from previously poisoned roaches. In the same preparations the muscle action potential seemed unchanged at least 1 hr later.

A few experiments with frogs confirmed the general picture. Injection of 5 γ /gm of ryanodine intraperitoneally caused the gradual appearance of a flaccid paralysis which was totally devoid of any excitation or central nervous symptoms. Unlike the situation in roaches, the flaccid stage in frogs was followed shortly by intense and enduring rigor. At the time a marked paralysis appeared in the anterior part of the frog, electrical stimulation of the pectoral and forelimb muscles failed to produce a local response, though the same stimulus reflexly produced flexion of the hind limbs. When the circulation to one leg was stopped by a ligature placed around the thigh prior to injection, electrical stimulation of other regions caused reflex movements in the ligated leg after muscles in the rest of the animal had lost their ability to contract. Thus, it appears that ryanodine affects contractile processes before excitation and conduction are impaired.

In order to investigate the direct action of ryanodine on muscle, rectus abdominis muscles of the frog were immersed in 5 ml of aerated saline containing ryanodine and the contractions recorded as in the method used for acetylcholine assay. Saline containing 10^{-4} ryanodine

produced a marked rigor-like contracture of the rectus muscle, which commenced 2 min after the muscle was first placed in ryanodine and reached a maximum in 30 min. With lower concentrations, to 10^{-8} ryanodine, the time of onset of rigor lengthened to 2.5 hrs, the height of contracture decreased, and the slope of the contracture curve became less. In the intact frog the ryanodine effect in the doses used was irreversible, whereas in the intact roach the effect of injection of 0.05 ml of 10^{-4} ryanodine was reversible, recovery occurring within 48 hrs. The rectus muscle of the frog, once it had started contracting, could not be brought back to the relaxed condition when washed with saline within 5 min of application of the ryanodine.

All evidence to this point indicates that ryanodine affects the contractile process before interfering with excitation or conduction. The site of action is then fairly well localized. What is the mode of action? Since the partial paralysis which results from ryanodine injection is tremorless and quite flaccid in the cockroach and frog (followed by rigor in the frog), the striking increase in oxygen consumption suggests that *Ryania* derivatives interfere with either the glycolytic processes or with the high-energy phosphate system in striated muscle. Preliminary experiments are under way to test the perfusate from ryanodinized muscles and to determine the influence of ryanodine on phosphagen and ATP hydrolysis and resynthesis.

Ryanodine solution which has caused rigor in a muscle (perfusate) has a more powerful rigor-producing effect than ryanodine alone. If a ryanodine solution which has caused rigor in a rectus muscle is drained off and applied to a second muscle, rigor begins with little or no latency, and the rate of attainment of complete rigor is more rapid. In one case, the ryanodine solution (10^{-8}) caused rigor to commence in the first muscle within 30 min, reaching a maximum in 135 min. Application of the perfusate from this muscle to a second caused rigor to commence almost immediately, attaining a maximum in 50 min. As is the case with ryanodine, ryanodine-muscle perfusate appears to be heat stable, and its effectiveness depends upon the original ryanodine concentration. The ryanodine perfusate also causes paralysis and a tremendous increase in oxygen consumption when injected into the intact roach, whereas saline-rectus perfusate and saline alone have no effect. There seem to be two possible explanations for this effect. Either contact with the muscle alters the ryanodine, rendering it more toxic, or ryanodine causes the production or release of material from the muscle which is responsible for the genesis of rigor. Though it is only possible to speculate on the nature of this effect, pronounced opacity of the muscles in a poisoned frog suggests that acid production is associated with ryanodine-induced rigor.

Injection of adenosine triphosphate (ATP) 10^{-8} in combination with ryanodine 10^{-4} shortened the interval preceding paralysis in the roach and frog. In the roach the time was decreased from 25 min for ryanodine alone to 6–8 min with ryanodine-ATP. ATP alone caused no apparent symptoms in the intact roach or frog. In the

frog, the ryanodine-ATP brought about an intense rigor within a few minutes, whereas ryanodine alone ordinarily causes rigor in 3-4 hrs. Ryanodine-ATP injections caused a 9-fold increase in oxygen consumption in the roach, and in one case, where the ATP had been warmed to 45° C and then cooled to room temperature before mixing with the ryanodine, the oxygen consumption was increased to 18 times normal following injection. In the intact roach the ryanodine-ATP effect was reversible in the concentrations used. In the intact frog and the rectus preparations the rigor produced was irreversible.

These results strengthen our belief that ryanodine acts specifically on the contractile process in striated muscle and indicate that the mode of action is probably one of interference with the phosphagen-ATP-ADP-actomyosin cycle during contraction.

References

1. CHADWICK, L. E., and HASSETT, C. Personal communication, 1947.
2. EDWARDS, G. A. Doctoral dissertation, Harvard Univ., 1947.
3. ROEDER, K. D., et al. *Science*, 1946, **104**, 425-426; *J. cell. comp. Physiol.*, 1939, **14**, 1-12; *Science*, 1946, **103**, 304-306; *J. Neurophysiol.*, 1947, **10**, 1-10.
4. SCHOLANDER, P. F. *Rev. sci. Instr.*, 1942, **13**, 32-33.

The Homing Tendency of Shad

EDGAR H. HOLLIS¹

Fish and Wildlife Service, College Park, Maryland

Two of the important problems in the study of shad populations along the Atlantic coast have been to determine to what extent shad return to the stream of their origin and to determine at what age they reach maturity. Shad are anadromous fish that enter the streams of the Atlantic coast in the spring to spawn, often migrating several hundred miles into fresh water for this purpose. It is known that the resulting young spend the first several months of their existence in fresh and brackish water, feeding and growing, and in the fall leave their fluvial environment for an unknown migration into the ocean, where they stay until maturity. That shad do return to the stream of their nativity has not been demonstrated. The age at maturity has received the attention of a number of investigators. Most have based their conclusions on scale markings, which they have recognized as being difficult to interpret.

Leim (4), reading markings believed to be winter rings on the scales from shad taken in the Shubenacadie River, placed the age of mature shad on these spawning grounds at at least 4 years; most he believed to be 5 years old or over, the maximum age being 8 or 9 years. Marks believed to be indicative of previous spawnings were noted on some of the scales.

¹ I wish to express appreciation to Robert A. Nesbit for his guidance in this experiment, to William C. Bunch, superintendent of the U. S. Fisheries Station, Edenton, North Carolina, and his staff for their assistance and interest, and to Ralph C. Hammer for his assistance in the tagging procedure.

Borodin (2) worked primarily with scales obtained from shad of the Connecticut River system. Because of the lack of distinctness of the annual marks, he counted the number of transverse grooves as well as annual marks—the number of complete transverse grooves divided by two being considered the true age when annuli were unreadable. Borodin concluded that a few male shad enter the rivers as 4-year-old fish, but that most of the males which he examined from the Connecticut River in 1941 were 5-7 years old. The females were determined to be 7 or more years of age. In addition, he pointed out the distinctiveness of the first and fourth annulus, comparing the latter to the "spawn marks" of salmon.

Barney (1) confirmed Borodin's observations, using otoliths. In a footnote (p. 57) Barney states that a single 3-year-old buck was taken from the Salmon River, but that this was unusual.

Greeley (3) examined scales collected from Hudson River shad and found great variance in the relative distinctness of annuli. He concluded that, though both roes and bucks may mature at 3 years, females in this age group were in the minority, and suggested as probable that "many fish of both sexes, but particularly roes, remain at sea during their third year and do not mature until four years old. It is entirely possible that a small percentage of these fish might be immature at an even greater age."

The lack of agreement in the various findings may be due to inherent differences in behavior of populations of the several streams or to differences of interpretation of scale markings for which experimental evidence is lacking. Obviously, the most direct method for interpreting scale markings and for determining age at maturity is to mark the young shad of known age and obtain scale samples from them at known intervals. This marking of young shad was attempted by Robert A. Nesbit and the author on several occasions, but the marking always resulted in the death of the young shad within a few days, presumably because of the injury inflicted in tagging and handling.

In 1941 I was able to tag successfully juvenile hatchery-reared shad by holding them in Ringer's solution, after tagging, until the incisions were healed. To date, three of the tagged fish have been reported. All of these were recaptured within a radius of 10 miles from their point of release, 3, 4, and 5 years after tagging.

The shad were pond reared at the U. S. Fish and Wildlife Service's hatchery located near Edenton, North Carolina. The eggs were collected and fertilized by standard hatchery procedure on April 24, 1941, placed in McDonald jars, and hatched in running water. On April 29, 1941, about 50,000 of the newly hatched fish were placed in a pond of 0.8 acre with a maximum depth of 5'. From then until October the shad were fed with a commercial fish food. On October 10 the pond level was gradually lowered to facilitate seining. The young shad were tagged from October 11 to 15. The fish at this time averaged about 10 cm in length.

The tag used was red celluloid, 20/1,000" thick, 9/16" in length, and 3/16" in width, with ends rounded.

on one side of the tag was printed a serial number and the notation "\$1.00 Reward," and on the reverse, "Fish and Wildlife, Washington, D. C." The printing was one in black.

The young fish were seined from the pond in lots of about 100, placed in a tub, carried about 125' to the site of tagging, dipped individually from the tub with a small net, and tagged. Great care was taken to avoid bruising them. They were picked from the net with wet cotton gloves, placed on a mat of soaked cotton, and held in place by the gloved hand during the operation. An incision was made into the abdominal cavity with a sharp, pointed, removable-blade scalpel just anterior to the vent and following the course of the myomeres. With fine-pointed forceps the tag was grasped by one end, the other end being inserted into the body cavity and pushed forward following the inner body wall. Each tagged fish was then placed in an adjacent tank of Ringer's solution.

The holding tanks were originally designed for the rearing of *Daphnia*. Each of these was made of concrete, measured 30' in length and 7' in width, and had a sloping bottom. The average depth of the filled tank was 1'. The Ringer's solution was prepared from the following formula: NaCl , 0.7%; KCl , 0.03%; CaCl_2 , 0.025%; NaHCO_3 , 0.003%.

The tagged fish were held in Ringer's solution until October 28, at which time they were seined from the tanks and released in Pembroke Creek, on which the hatchery is located, $\frac{1}{2}$ mile above its mouth.

Over the 5-day period 2,466 fish were marked. During the holding time (13-17 days) 1,388 fish died or lost their tags (56.3% mortality). From the 1,078 fish released, three returns have been made.

Not all of the fish tagged (and presumably released) were shad. Among the tagged fish which died during the holding period a number of specimens were found which proved to be the young of river herring. These, in all probability, were introduced into the rearing pond as eggs when the pond was filled. No tags have been returned from river herring.

The particulars of the tagged shad recovered are given below.

(1) A shad bearing tag number 1057 was caught April 17, 1944, in Albemarle Sound, two miles below Chowan River bridge. The finder told me that he had caught the fish himself in a haul seine and had cleaned the fish and disposed of the offal before noticing the tag adhering to the body wall, held in place by a thin, transparent membrane. He could not recall the sex of the shad at the time I talked with him, but he stated that the shad was small and "spawned out."

(2) A roe shad bearing tag number 1412 was caught March 22, 1945. This fish was purchased by an Edenton, North Carolina, housewife from a fisherman operating at Skinner's Point on Albemarle Sound. The tag was embedded in a roe and was not noticed until the roe had been cooked and was being divided for serving.

(3) Tag number 539 was found lying free between the roes of a shad purchased from a haul seiner operating in the Chowan River near Edenton, North Carolina. This shad was caught April 3, 1946.

One other tag discovery has been reported from Skinner's Point, but this discovery is unsubstantiated by the return of the tag itself.

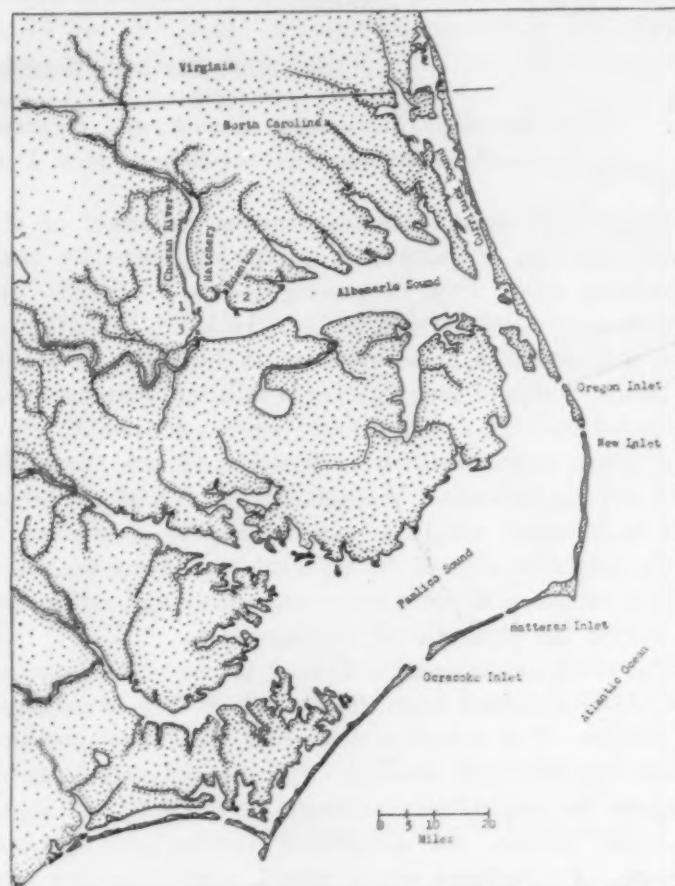


FIG. 1

Unfortunately I was unable to obtain scales from any of the three fish mentioned above and therefore was unable to determine the nature of the scale markings. Spawning marks appear to be formed by the absorption of part of the anterior periphery of the scale at the time the shad enters fresh water to spawn. This mark shows up in strong contrast to that portion of the scale deposited between spawning migrations. Had scales been available from these returned fish, it should have been possible to determine whether they were recaptured on a first or a subsequent migration.

The fact that all of the returns were made from the immediate vicinity of the place at which the young shad were released and that no returns were made from other areas in this complex system of waterways (Fig. 1) is consistent with the theory that shad do return to the stream of their nativity.

References

1. BARNEY, R. L. In *A report of investigations concerning shad in the rivers of Connecticut*. Hartford: State Board of Fisheries and Game, 1925. Pt. III, pp. 52-60.
2. BORODIN, N. In *A report of investigations concerning shad in the rivers of Connecticut*. Hartford: State Board of Fisheries and Game, 1925. Pt. II, pp. 46-51.
3. GREELEY, J. R. In *A biological survey of the lower Hudson watershed*. Albany: State of New York Conservation Department, 1937. Pp. 45-103.
4. LEIM, A. H. *Contributions to Canadian biology*. (Vol. II.) Toronto: Biological Board of Canada, Univ. Toronto Press, 1924. Pp. 163-284.

Effect of Antiserum and Prolonged Cultivation on the Agglutinative Characteristics of a Type I Meningococcus

DOROTHY NEUHOF NAIMAN¹

Department of Physiology, Health, and Hygiene,
Hunter College of the City of New York

The present communication reports the effect of different methods of cultivation on the agglutinative characteristics of a Type I meningococcus. Whether any change that occurred was to be considered indicative of S to R dissociation or as evidence of the apparent ability of many strains of meningococcus to alter their antigenic characteristics (2, 5, and others) was questionable. However, these experiments were based upon the possibility that the agglutinative characteristics of a strain which had maintained antigenic constancy over a number of years might be altered by cultural conditions known to induce variation in some other organisms and shown also to reduce the virulence of meningococci.

The stock culture was a Type I strain of meningococcus (44F) obtained from the New York City Department of Health. This strain was selected from among several which agglutinated to high titer in polyvalent serum because, in preliminary attempts to produce an agglutinative variant, its substrains showed the greatest change. It produced small, round, slightly yellow colonies with smooth surface and even borders; there was no evidence of secondary colony formation. According to Rake's description (6), it was a "stock" strain. After 9 serial subcultures of single colonies, at 48-hr intervals, during which time no morphological change was observed, it was maintained as the stock culture on 1% glucose agar.

Schwartzman (7) has reported loss of toxigenicity of meningococci maintained on egg media, and Cohen (1) found that both virulence and precipitative activity of "stock" strains were decreased by subculture in semi-fluid agar. Enders (3) has reported S to R dissociation of meningococci which were repeatedly subcultured in defibrinated rabbit blood; however, Rake (6), in repeating the work, felt that the observed changes were, rather, analogous to those found when recently isolated strains are maintained on artificial media and that the strains tended to die out after two or three subcultures in this medium, before true R variants appeared. Of the various methods which suggested themselves as possible incitants to agglutinative variation, the following were selected as being most feasible for this work: (1) Dorset's egg medium, sealed with paraffin, transplanted monthly; (2) 1% glucose semisolid agar containing polyvalent antimeningococcus serum, transplanted weekly; and (3) 1% glucose broth containing polyvalent antimeningococcus serum, transplanted on alternate days.

¹This work was performed in the Department of Bacteriology, New York University College of Medicine. The author wishes to record her sincere appreciation for the guidance of the late Dr. Maurice Brodie.

Agglutination tests were performed with saline suspensions of 18- to 20-hr cultures as antigen. After 2 hr at 56° C and 18 hrs in the refrigerator, the results were read by macroscopic inspection. Agglutinin absorption

TABLE 1
AGGLUTINATION REACTIONS WITH HOMOLOGOUS AND DERIVED STRAINS

Serum Antigen	Dilutions of serum						
	1-40*	1-320	1-640	1-1,280	1-2,560	1-5,120	1-10,240
320†	St	4	4	4	4	2	1
	E ₃	4	4	4	4	3	..
	A ₇	4	4	4	3
	AA ₈	4	4	4	4	4	4
	B ₄₄	4	4	4	3	1	..
321†	St	4	4	4	3	2	..
	E ₃	4	4	4	4	2	..
	A ₇	4	4	3	2
	AA ₈	4	4	4	4	3	3
	B ₄₄	4	4	4	4

* The numerals under each serum dilution represent degree of agglutination visible macroscopically in strong light.

† Serum prepared with stock strain as antigen.

Explanation of strain designations: St = stock strain, E = strain cultured in egg medium, A = strain cultured in semisolid agar containing 10% antiserum, AA = strain cultured in semisolid agar containing 20% antiserum, B = strain cultured in broth containing 10% antiserum. The subscripts represent the number of passages in the medium.

tests were carried out under the same temperature conditions, the absorbing antigen being the washed packed cells thrown down from saline suspensions previously maintained at 60° C for 1 hr. Serum against the stock

TABLE 2
AGGLUTININ TITER OF SERUM PREVIOUSLY ABSORBED WITH HOMOLOGOUS AND SUBSTRAINS

Serum	Antigen	Dilutions of serum						Absorption control (%)
		1-20	1-40	1-80	1-160	1-320	1-640	
Unabsorbed	St	4	4	4	4	4	4*	..
Absorbing	strain							
	St	4	4	3	97
	E ₃	4	4	4	97
	A ₇	4	4	2	1	97
	AA ₈	4	4	2	97
	B ₄₄	4	4	3	2	1	..	87.5

* Final titer = 1-5,120.

strain was obtained from rabbits which had received intravenously, at 24-hr intervals, 3 injections of heat-killed organisms, followed, after a week's rest, by 3 injections of live organisms from 18-hr cultures. The serum was

ained by heart puncture 6 days after the final infection.

Table 1 gives the agglutinative titer of the substrains sera prepared against the stock strain, while Table 2 shows the results of agglutinin absorption tests performed with samples of serum, each of which had previously been absorbed with one of the substrains.

During the course of the work there was no observable change in cultural or fermentation reactions.

Of the substrains derived from a stock culture apparently stable in agglutinative potency, only those cultivated in the presence of 10% antiserum gave any evidence of change in agglutinogenic property. While the change in titer was not great, the fact that the parent strain had been maintained for a number of years without change in antigenic characteristics may give reason to believe that further cultivation in the presence of antiserum might produce greater change. This possibility is indicated by the fact that the strain which had gone through 44 generations showed greater loss than the one which was observed through only 7 generations. Should further changes occur during prolonged cultivation the results would confirm the report of Evans (4), who attributed the spontaneous appearance of an R variant of a Type III stock strain to the presence of antibody in the human blood used for the medium on which it was cultivated.

References

COHEN, S. M. *J. Immunol.*, 1936, **30**, 203-211.
DOPTER, C. *Rév. Hyg.*, 1940, **61**, 513-529.
ENDERS, J. F. *J. Bact.*, 1932, **23**, 93-95.
EVANS, F. L. *J. Bact.*, 1947, **54**, 175-177.
KIRKBRADE, M. B., and COHEN, S. M. *Amer. J. Hyg.*, 1932, **15**, 444-458.
RAKE, G. *J. exp. Med.*, 1933, **57**, 549-559.
SCHWARTZMAN, G. *J. inf. Dis.*, 1931, **48**, 339-349.

The Inactivation of Invertase by Tyrosinase

IRWIN W. SIZER¹

Department of Biology,
The Massachusetts Institute of Technology

The problem of the inactivation of an enzyme by the action of oxidases on certain groupings in the enzyme protein was raised by Sizer (5), who demonstrated that a fraction of the tyrosyl groups of certain proteins could be oxidized by tyrosinase. In view of the importance of tyrosyl groups for the activity of most biologically active proteins (4), it seemed possible that certain enzymes might be oxidatively inactivated by tyrosinase. No effect of tyrosinase on enzyme activity could be demonstrated (2, 5), however, for the proteases pepsin, trypsin, and chymotrypsin. Despite these negative results, it seemed wise to investigate further the possible control of one enzyme system by another. In the initiation of this problem we have studied the action of mushroom tyrosinase on yeast invertase.

¹The author is grateful to Mr. John Fenessey and Miss Janette Robinson for their assistance in this study.

In a typical experiment, 0.5 ml of tyrosinase (Treemond, 3,500 Miller and Dawson units/ml) is incubated with 0.1 ml of diluted invertase² (1), 0.5 ml of M/20 phosphate buffer, pH 6.0 and 0.5 ml of water plus toluene for 18 hrs at 37° C. A control experiment, run simultaneously, is identical except for the fact that the tyrosinase has been inactivated by boiling. In certain ex-

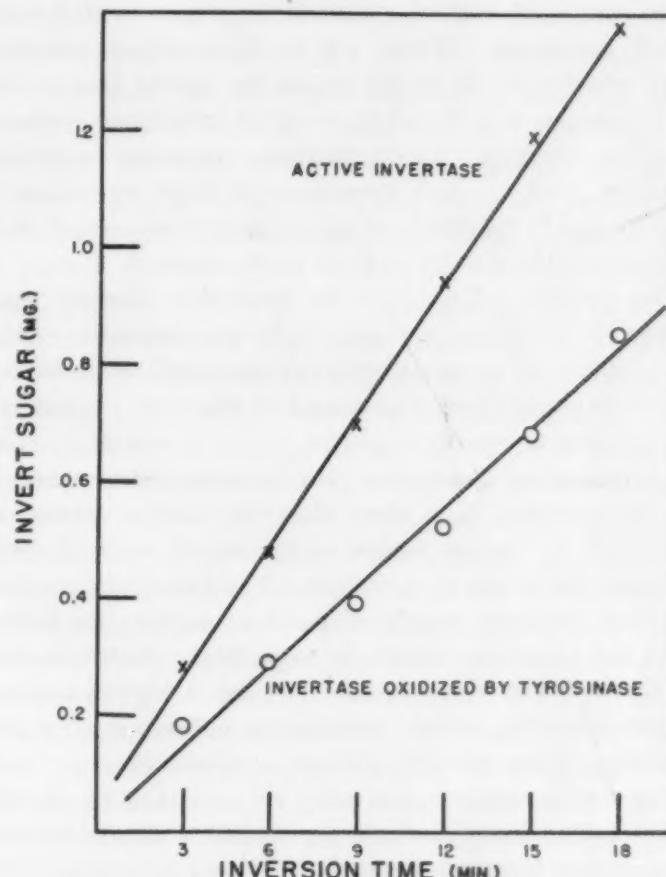


FIG. 1. The formation of invert sugar from 6% sucrose at pH 6.0 at 37° C in the presence of 0.004% Dieu invertase is plotted as a function of the inversion time. The "active invertase" had been treated previously with boiled Treemond tyrosinase for 18 hrs at 37°, while the "invertase oxidized by tyrosinase" had been incubated with active tyrosinase for the same time.

periments both control and experimental solutions were placed in Cellophane sacs and dialyzed continuously during the reaction against the phosphate buffer. After incubation with tyrosinase the residual activity of the invertase was measured. The samples were diluted to 5 ml with buffer (at 37° C) and at zero time were rapidly mixed with 5 ml of 12% sucrose. One-ml samples were removed at successive time intervals and added to 3 ml of dinitrosalicylic acid reagent for reducing sugars (6). The intensity of color developed after heating the solutions in the usual way (6) was measured at 575 m μ with the Coleman Universal Spectrophotometer and converted to milligrams of invert sugar. Typical results are presented in Fig. 1, from which it appears that the liberation of invert sugar from sucrose by invertase follows zero-

²The author is most grateful to Hector Dieu, University of Liège, for a generous sample of high-purity invertase. The invertase solution had a time value of about 0.30 min and contained 0.20 mg of nitrogen and 0.40 mg of carbohydrates/ml. It was diluted 250 times before use.

order kinetics reasonably well during the initial phase of the hydrolysis. Rates are calculated from the slopes of the straight lines fitted to the points and, when compared, show that the invertase oxidized by active tyrosinase has only 57% of the activity of the control invertase which had been treated with boiled tyrosinase.

In more than 100 experiments using purified preparations of tyrosinase the invertase was inactivated 10-40% when compared with the control invertase treated with boiled tyrosinase. While all yeast invertase preparations, whether crude or highly active, can be inactivated by tyrosinase, it is found that not all tyrosinase preparations are effective. Crude tyrosinase does not inactivate invertase, and purified tyrosinase of high "cresolase" activity has little effect, while purified tyrosinase of high "catecholase" activity³ (3) is most effective.

The question of whether the tyrosinase directly inactivates the invertase, or converts by oxidation impurities (or products of protein autolysis) to invertase inhibitors, cannot be satisfactorily answered at this time. Since the phenomenon is equally apparent if continuous dialysis of the solutions of tyrosinase plus invertase occurs during the inactivation, it is clear that the results cannot be accounted for by an action of tyrosinase on dialyzable potential inhibitors of invertase. The fact that invertase in many different stages of purification may be inactivated by tyrosinase makes it more likely that invertase is inactivated directly rather than by a high-molecular-weight impurity, which becomes an inhibitor after the oxidation of its phenolic groups by tyrosinase.

The results might conceivably be explained on the hypothesis that the tyrosinase preparations merely contain an invertase inhibitor which is destroyed by boiling. To test this idea it is necessary to employ some means other than boiling to prevent the action of tyrosinase in the control experiment. This can be done by excluding oxygen from the control by bubbling nitrogen through the control solution and then evacuating it at the water pump. An equally effective method is to bubble continuously through the control solution hydrogen activated with platinized asbestos.⁴ Results with both techniques are comparable to those with the usual method using boiled tyrosinase and show that the inactivation of invertase by tyrosinase is not explained by the tyrosinase preparation acting as an inhibitor. These experiments also show the dependence upon oxygen of the inactivation reaction. Experiments are now in progress to correlate the loss in activity of the invertase oxidized by tyrosinase with chemical and physical changes in the invertase molecule.

These preliminary results show that yeast invertase can be partially inactivated by incubation with mushroom tyrosinase. This inactivation is best explained on the

³ Both the "cresolase" and the "catecholase" preparations of tyrosinase were generously supplied by C. R. Dawson, of Columbia University.

⁴ This technique is not applicable to highly purified Dieu invertase, which is partially inactivated by activated hydrogen.

basis of an oxidation of essential tyrosyl groups in the invertase molecule by tyrosinase.

References

1. DIEU, I. H. *Bull. Soc. Chim. Belg.*, 1947, 55, 306.
2. EDMAN, P. *J. biol. Chem.*, 1947, 168, 367.
3. MALLETT, M. F., LEWIS, S., AMES, S. R., NELSON, J., and DAWSON, C. R. *Arch. Biochem.*, 1948, 16, 23.
4. OLcott, H. S., and FRAENKEL-CONRAT, H. *Chem. Ind.* 1947, 41, 141.
5. SIZER, I. W. *J. biol. Chem.*, 1946, 163, 145; 1947, 163, 303.
6. SUMNER, J. B. *J. biol. Chem.*, 1925, 63, 393.

Mammary Carcinoma in Female Rats Fed 2-Acetylaminofluorene¹

R. W. ENGEL and D. H. COPELAND

Laboratory of Animal Nutrition
Alabama Agricultural Experiment Station
Alabama Polytechnic Institute, Auburn

In connection with studies concerning the relation of nutrition to cancer it was observed that mammary tumors developed consistently in from 3 to 6 months in all female rats receiving diets containing .03% 2-acetylaminofluorene. This observation has been confirmed in several experiments, results of which are reported in this paper.

Piebald female rats of the Alabama Experiment Station (AES) strain were used for these studies. The animals were placed on the experimental diets at 23 days of age, at weights of 35 to 50 gm. They were cage-individually on screen floors and fed daily *ad libitum*.

The composition of the diets used in these studies is given in Table 1. Two dietary modifications—omission of choline and the addition of iodinated casein—were tried, but these did not influence the results, as can be seen from the summary data in Table 2.

A period of about 16 weeks was required for the animals to attain a body weight of approximately 250 gm. This amount of gain is normally made in 6-8 weeks when these diets are fed without carcinogen.

Twenty-four of the 25 female rats fed the carcinogen diets developed palpably detectable mammary tumors between the 95th and 181st day of the experiment. One animal died of unknown causes during the third month of the experiment, at which time no tumors were detectable in any of the animals. The animals were killed and autopsies were made, usually within one or two weeks.

¹ Published with the approval of the director, Alabama Agricultural Experiment Station. This work was supported in part by grants from the Nutrition Foundation, Inc., New York City, and from the American Cancer Society on the recommendation of the Committee on Growth of the National Research Council. A preliminary report of this work was presented before the 39th Annual Meeting of the American Association for Cancer Research at Atlantic City, New Jersey, March 13, 1948.

The authors are indebted to H. L. Stewart, senior pathologist, National Cancer Institute, for assistance in the interpretation of the microscopic material.

After a mammary tumor was detected by palpation. At autopsy, multiple mammary tumors were observed in and single tumors in each of the remaining 10 animals.

TABLE 1

PERCENTAGE COMPOSITION OF BASAL DIETS*

Ingredient	Diet No.	
	C-5	C-20
Wheat-extracted casein	9.00	6.00
Wheat-extracted peanut meal	0.00	30.00
Germinated corn grits	20.00	0.00
Cornstarch	51.70	39.90
Yeast mixture	4.00	4.00
Salt	14.00	19.00
Cod-liver oil	1.00	1.00
Cystine	0.30	0.10
Acetylaminofluorene	.03	.03

* Each kg of basal diet was fortified with the following (mg): α -tocopherol, 50; thiamine, 2; pyridoxine, 2; riboflavin, 4; pantothenate, 10; niacin, 20; β -inositol, 200; and choline, 2,000. The authors are indebted to Merck & Co., Inc., New Jersey, for these vitamins.

A total of 82 mammary tumors were removed and prepared for microscopic examination. These ranged in size from small, barely palpable knots of firm tissue to growths up to 3 or 4 cm in diameter and were distributed in all

TABLE 2

100% INCIDENCE OF MAMMARY TUMORS IN FEMALE RATS FED 2-ACETYLAMINOFLUORENE

Litter No.	No. of animals	Average body weight (gm)	No. of animals with mammary tumor*	Tumor induction period (days)	
				Initial	16 weeks
24-14	2	44	156	2	141
24-14	2	47	193	2	151
24-35	4	36	198	4	128
25-11	5‡	47	203	4	115
25-20	5	47	221	5	128
26-32	4	42	223	4	151
25-29	1	49	218	1	152
25-18	1	45	233	1	146
24-25	1	35	190	1	152

* The total number of mammary tumors distinctly visible at autopsy in the 24 animals was 82, the largest number appearing in any one animal was 10, and a single mammary tumor was present in each of 10 animals.

† Choline was omitted from the diet.

‡ One of these animals died after 86 days on experiment. No tumors were observed and the cause of death was undetermined.

§ The diet was supplemented with iodinated casein (.2% /kg of diet). The authors are indebted to the Cerophyl Laboratories, Inc., Kansas City, Missouri, for this material.

¶ Tumors of the mammary region. On the basis of microscopic examination, the tumors were diagnosed as mammary carcinoma in all cases. Metastases to the lungs

were observed in a few cases, and in one case a primary carcinoma was also present in the external auditory canal.

So far as is known, a uniform production of mammary tumors in the rat has not been previously reported. Whether this unusual result is related to the age or strain of animal or the type of diet used is not known. No significant litter differences were observed in this strain.

Wilson and associates (6), who first demonstrated the carcinogenicity of 2-acetylaminofluorene, observed mammary tumors in 40% of female rats fed the compound at a level of .031% of the diet. Bielschowsky (1) noted a much higher incidence (60%) of mammary tumors with this compound in female rats of a Wistar substrain than in piebald females (4%). Harris (5) likewise observed a high incidence (40-75%) of mammary tumors in Wistar female rats fed this compound. Cantarow (3), working with the Sherman strain, and Dunning (4), comparing 5 other strains, both observed a low incidence of mammary tumors. In summarizing the reported investigations, it is apparent that a relatively high incidence of mammary tumors in female rats was observed only in animals descendant of the Wistar strain. It should be pointed out, however, that a comparison of reported results hardly seems valid until the relation of nutritional factors to the carcinogenicity of 2-acetylaminofluorene has been more thoroughly investigated. With the exception of the work of Harris (5), in which purified diets were used, the previously reported investigations with this compound have involved diets composed of natural foodstuffs. In the present study, semipurified diets were used. Bielschowsky (2) has reported that a yeast supplement in a diet of bread and skim-milk powder markedly reduced the mammary tumor incidence. On the other hand, Wilson and associates (7) have recently reported no change in the incidence or time of development of tissue changes induced by 2-acetylaminofluorene by enriching the diet with cod-liver oil, yeast, and wheat germ.

Investigations are under way to evaluate more carefully the relation of specific dietary factors to the carcinogenicity of this compound. A more detailed report of the pathologic tissue changes observed in these studies is being prepared. The ease with which the mammary tumor can be detected and the assurance herein demonstrated that this type of tumor will appear consistently under controlled dietary conditions should make this a reliable experimental approach to the problem.

References

1. BEILSCHOWSKY, F. *Brit. J. exp. Path.*, 1946, **XXVII**, 135.
2. BEILSCHOWSKY, F. *Brit. J. Cancer*, 1947, **1**, 146.
3. CANTAROW, A., PASCHKIS, K. E., STASNEY, J., and ROTHENBERG, M. S. *Cancer Res.*, 1946, **6**, 610.
4. DUNNING, W. F., CURTIS, M. R., and MADSEN, M. E. *Cancer Res.*, 1947, **7**, 134.
5. HARRIS, P. N. *Cancer Res.*, 1947, **7**, 88.
6. WILSON, R. H., DEEDS, F., and COX, A. J. *Cancer Res.*, 1941, **1**, 595.
7. WILSON, R. H., DEEDS, F., and COX, A. J. *Cancer Res.*, 1947, **7**, 450.

IN THE LABORATORY

A Simple Micro-Beaker for Use With the Beckman pH Meter (Model G)

VICTOR H. DIETZ

Department of Bacteriology and
The W. K. Kellogg Foundation Institute of
Graduate and Postgraduate Dentistry,
University of Michigan, Ann Arbor

It is often necessary in certain microbiological procedures to determine the pH of a minute quantity of a fluid which may not possess a sufficient buffer capacity to permit dilution to the minimal quantity of approximately 2 ml, as required in the ordinary specimen cup (5-ml beaker). Other procedures, occasionally requiring subsequent analyses on the same minute amount of specimen, may not permit of dilution despite the inherent buffer capacity. The use of the device to be described permits one to make more frequent tests on such substances as tears, sweat, salivary aspirate, and other normal as well as pathological fluids ordinarily obtainable

serviceable height. A $\frac{1}{16}$ " and a $\frac{1}{4}$ " round surgical bur were used to cut the circular depressions to the depth shown. The channel between the depressions is cut with a $\frac{1}{8}$ " round bur (surgical or dental). The channel, of course, establishes the necessary bridge between the electrodes at the expense of a negligible amount of the specimen. The depressions and channel are polished with a wisp of cotton wound around the burs employed, using extra fine pumice and water. A thin paste made of SnO_2 in water produces a lustrous and smooth finish. Various hand rotor devices or the dental engine serve admirably in performing these operations. In order to avoid depolarizing the surface of the plastic the cutting procedure should not be performed too rapidly, and even greater discretion should be employed in avoiding the generation of heat in polishing. The entire device may be smoothed and polished with the same agents, using a polishing wheel of medium size. This design is applicable to the Beckman "270" calomel electrode and the "290" glass electrode, which are most commonly employed with the instrument.

The total volume of the depressions and channel should not exceed 0.2 ml. However, 0.1 ml of the specimen may be expediently employed due to the combined displacing volumes of the two electrodes. A simple procedure is to place a drop, or about 0.05 ml, in each depression, place the micro-beaker in the specimen-cup support (beaker holder), loosen both electrode set screws, and carefully elevate to position. The calomel electrode should follow the path of straight-line insertion, the glass electrode being converged toward it. The comparatively soft and resilient surface of the plastic greatly minimizes the danger of breaking or scratching the electrodes. The bridge will automatically be formed if the fluid should not be inordinately viscous. Care should be taken with viscous solutions, however, for if any is trapped in the smaller depression, connection with the porous fiber of the immersion tip of the calomel electrode cannot be established. The diameter of the micro-beaker being less than that of the cup support (beaker holder) ensures simple flexibility in adjustment. The use of this device does not require the removal of the regular glass electrode, or the 5-ml beaker holder, and one work may immediately follow another using the micro-beaker or conventional cup without inconvenience. The temperature variable is no more critical with 0.1 ml of a specimen than with a larger amount.

The plastic is entirely resistant to acid or alkali within the usual pH range (2-10). It is readily attacked by the organic solvents and crazes rapidly by short exposure to 70% alcohol. The micro-beaker is best cleaned with a soft brush or towel, using warm water, soap, or any of the detergents. It may be disinfected, if necessary, by immersion in a 1:1,000 solution of bichloride of mercury for 10 min or a 1:1,000 solution of benzalkonium chloride.

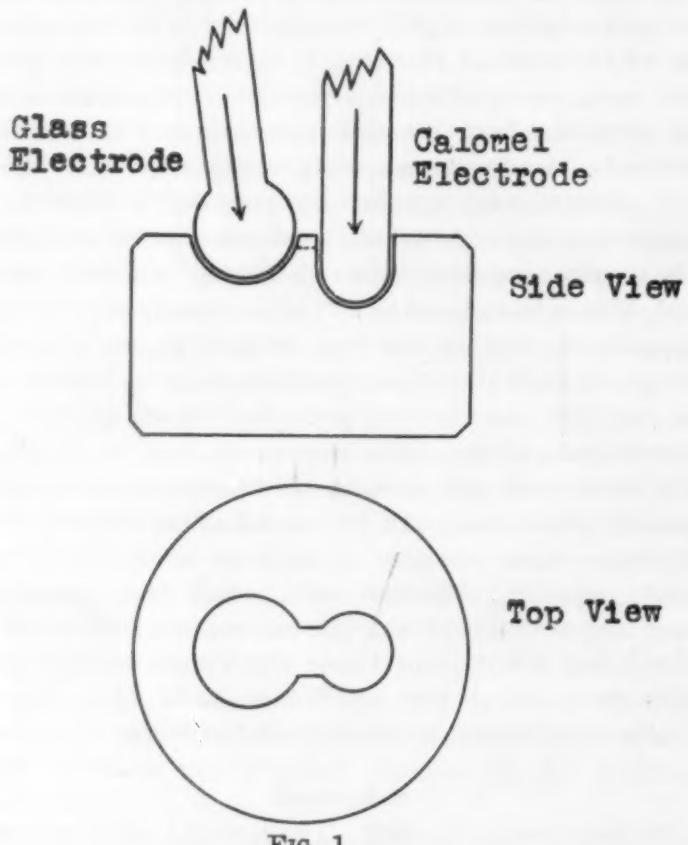


FIG. 1

in only limited quantities. Certain clinical and pediatric specimens of but a single drop in quantity may be accurately determined in only a fraction of the time that is usually required for a microcolorimetric test.

The micro-beaker shown in Fig. 1 was cut from a $\frac{1}{4}$ " cast Lucite rod. Plexiglas, a virtually identical methyl methacrylate product, may also be used for this purpose. A length of $\frac{1}{2}$ " is cut from the rod and affords a most

loride (U.S.P.) for 20 min. Because of the aforementioned effect that alcohol has upon the plastic, tinctures must necessarily be avoided. Boiling of the device causes early depolymerization and is therefore inadvisable. The $\frac{1}{2}$ " height of the device permits the intact removal and subsequent replacement of the specimen cup without replenishment of the distilled water or buffer solution in which the electrodes are ordinarily maintained.

When testing minute quantities by this method it is particularly desirable that the electrodes and microtweaker be scrupulously clean and adequately rinsed. The electrodes are ideally rinsed three times and blotted with a fresh sheet of cleansing tissue. This procedure is especially recommended if the specimen should be poorly buffered. For a very critical test a contact discrepancy in readings may be avoided by employing the device with the preferred buffer solution when making the asymmetry potential corrections. It is also preferable to use a buffer solution of approximately the same pH value as the solution being tested. The plastic is comparable to soft glass as a nonconductor, possesses less porosity, and is virtually unbreakable.

A Rapid Method for Preparing DDT in the Laboratory¹

JOSEPH M. GINSBURG

New Jersey Agricultural Experiment Station,
Rutgers University, New Brunswick, New Jersey

DDT is an abbreviation of the chemical term, dichlorophenyl-trichloroethane, $(C_6H_4Cl)_2CHCCl_3$. This outstanding new insecticide has become, during the last 5 years, the subject for numerous investigational studies in the entomological and chemical fields. The commercial technical-grade DDT is a mixture of several isomers and impurities (3). It consists essentially of 70-75% of *p,p'*-DDT, 1-trichloro-2,2-bis (*p*-chlorophenyl) ethane. The *p,p'*-DDT isomer is mainly responsible for the insecticidal properties of the compound. When pure, it has a melting point of 108°-109° C.

Commercially, DDT is now prepared by the Baeyer condensation method originally employed by Zeidler (5), who was the first to report the synthesis of this compound. The process involves the use of chloral, fuming sulfuric acid, expensive and more or less complicated apparatus (4). Both chloral and fuming sulfuric acid are unpleasant and hazardous to handle, especially by inexperienced workers and students. Recently a laboratory method was suggested by Darling (2) in which chloral hydrate is substituted for chloral but requires the addition of oleum.

Research work with DDT, as well as teaching insecticides, often requires the synthesis of small quantities of pure DDT in the laboratory. Not all laboratories are equipped with suitable apparatus to handle hazardous reagents. The writer, being confronted with such a

problem, has worked out a short and simple method for preparing small quantities of DDT without the use of either chloral or fuming sulfuric acid. The entire process can be carried out within one laboratory period and has been successfully used during the last two years by the writer and graduate students taking courses in insecticides.

The method is based on the theoretical reaction of 1 gm mole of chloral hydrate and 2 gm moles of chlorobenzene (sp.gr., 1.107) in the presence of about 4-5 times their combined volume of concentrated sulfuric acid.

When only small quantities of DDT are desired, correspondingly smaller proportions of ingredients, based on 0.1 gm mole of chloral hydrate, such as 17 gm of chloral hydrate and 23 ml of chlorobenzene, are convenient to use.

The procedure is as follows:

Place 17 gm of chloral hydrate crystals and 23 ml of chlorobenzene in a glass-stoppered, 500-cc Pyrex reagent flask and keep in electric oven at 60°-70° C for about 20-30 min with occasional shaking, or until all the crystals have dissolved. Cool to room temperature and slowly add about 180 ml of concentrated H_2SO_4 . Stopper and shake vigorously until precipitation starts. This operation usually requires about 1 hr. Let stand for about 15 min with frequent shaking or until precipitation is complete. The upper solid layer contains the crude DDT.

Pour the mixture into a glass jar containing about 1 gal of cold tap water and allow to stand for 15 min, or until the solids have settled. Filter through three layers of cheesecloth and wash several times with tap water. Transfer residue from cheesecloth into a wide-mouth bottle or a small glass jar, add about 50 ml of either 2% Na_2CO_3 or 4% $NaHCO_3$ solution, and shake for 5-10 min. This will neutralize the acidity.

Filter through a small, dry, Buchner funnel and wash several times with distilled water, or until the filtrate is neutral to litmus. Continue air suction for a few minutes or until no more water drains out. Transfer the residue to a small porcelain mortar, add about 100 ml of ethanol, and triturate with a pestle for 5-10 min. Filter through a dry Buchner funnel, rinsing twice with 25 ml of ethanol. Continue suction until no more alcohol drains out.

Dry the residue at 70°-75° C in an electric oven for 2 hrs, or until all the alcohol has volatilized. Cool to room temperature and weigh. An average yield of about 16 gm of practically pure DDT is obtained.

Samples from 6 batches prepared during the last two years were analyzed for *p,p'*-DDT by the chemical method developed by Cristol, Hayes, and Haller (1). The results have shown variations of from 94.5 to 98.35% *p,p'*-DDT, giving an average of 96.82%. The melting point ranged from 106° to 108° C.

The laboratory-prepared DDT was tested on third-instar larvae of *Aedes aegypti* in comparison with a commercial sample of DDT (technical grade). The tests were made in beakers, each containing 200 ml of distilled water and about 50 larvae. One ml of ethanol containing various concentrations of the toxicants was dispersed in each beaker. Each concentration was run in triplicate, giving a minimum of 150 larvae per test.

¹ Paper of the Journal Series, New Jersey Agricultural Experiment Station, Rutgers University, Department of Entomology.

At the end of 48 hrs the dead and live larvae were counted. During this period some of the larvae had pupated, and the live pupae were included with the surviving larvae. The results given in Table 1 indicate that

TABLE 1
COMPARATIVE TOXICITY OF LABORATORY-PREPARED DDT AND COMMERCIAL DDT TO LARVAE OF *Aedes aegypti*

Dilution (ppm)	Per cent larvae dead in 48 hrs			
	Laboratory		Commercial	
	Total No. larvae	Dead (%)	Total No. larvae	Dead (%)
0.1	156	100	158	100
0.05	152	100	170	100
0.025	176	100	160	95
0.0125	161	85	153	75
0.010	175	62	165	50
Check (1 cc of ethanol)	160	4		

the laboratory-prepared DDT is at least as toxic to mosquito larvae as is the commercial DDT. At dilutions of 0.05 ppm both samples gave 100% dead larvae. In dilutions of 0.01 ppm the commercial sample gave 50% kill, as compared with 62% kill for the laboratory sample.

References

1. CRISTOL, S. J., ROBERT, A. H., and HALLER, H. L. *Ind. eng. Chem. (Anal. ed.)*, 1945, **17**, 470.
2. DARLING, S. F. *J. chem. Educ.*, 1945, **22**, 170.
3. HALLER, H. L., et al. *J. Amer. chem. Soc.*, 1945, **67**, 1591.
4. MOSHER, H. S., et al. *Ind. eng. Chem.*, 1946, **38**, 916.
5. ZEIDLER, O. *Dtsch. chem. Ges.*, 1874, **7**, 1180.

Radiocardiography: A New Method for Studying the Blood Flow Through the Chambers of the Heart in Human Beings

MYRON PRINZMETAL, ELIOT CORDAY,
H. C. BERGMAN, LOIS SCHWARTZ, and RAMON J. SPRITZLER

*Institute for Medical Research,
Cedars of Lebanon Hospital, Los Angeles¹*

The passage of radioactive substances through the cardiac chambers can now be graphically recorded with the aid of a specially constructed, ink-writing Geiger-Müller counter. This procedure makes it possible to investigate in human beings certain hemodynamic functions not previously accessible to study. Briefly, the method consists of placing a carefully shielded Geiger-Müller tube over the precordium, rapidly injecting 0.1-0.2 mc of radiosodium (Na^{24}) into one of the antecubital veins, and recording the counts by means of the newly devised direct-writing counter.² The curve records the concen-

¹ Endowed by grants from the Blanche May and Beaumont Research Funds.

² We wish to thank Dr. Robert Miller, of Los Angeles, for the design and construction of the apparatus.

tration of radiosodium in the structures underlying the tube, as represented by the number of disintegrations of the radioactive element per unit of time. The curve is corrected for the random bursts of radiosodium by taking the mean of the counts over a half-second period. Na^{24} has a short half-life (14.8 hrs) and is rapidly eliminated from the kidneys. The quantity injected is within the safe range recommended by the authorities, and the amount of radiation is much less than that which the patient receives during various diagnostic X-ray examinations. In the last year and a half, more than 250 subjects were given injections for radiocardiography without untoward effects.

The reconstructed precordial tracings in normal subjects generally consist of two principal waves connected by a plateau-like transitional zone. The tracings read from right to left, the injection point being at the far right. For purposes of simplicity, the first wave, which traces the blood through the chambers of the right heart, has been called the R-wave, while the second wave may be termed the L-wave, as the left heart receives and expels the labeled blood.

The initial upsweep of the curve is preceded by a long stretch at the base line. This is the period following the injection during which no radioactivity is detected over

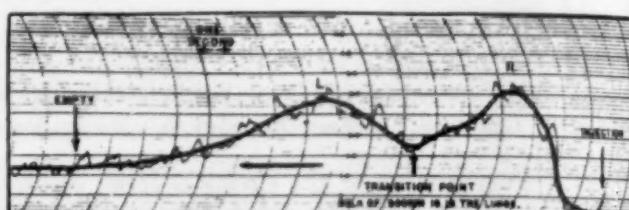


FIG. 1. Radiocardiogram of normal patient. Note characteristic biphasic wave as heart pumps the radioactive blood through its chambers. Each vertical line denotes a 1-sec interval. (Tracing is read from right to left.)

the chest and represents the time interval required for radioactive blood to travel from the site of injection to the precordium. At the termination of this period, the tracing begins to sweep upward to reach the peak of the first wave. This records the entrance of the blood into the superior vena cava, right auricle, and right ventricle. The curve then descends because of the expulsion of the labeled blood from the right heart into the lungs. The line then rises as blood returns from the pulmonary circulation and enters the chambers of the left side of the heart. After the second peak has been reached, the curve descends gradually and ends in a second plateau which lies above the base line. The long descending limb of the L-wave represents the period during which the left cardiac chambers are being emptied of the labeled blood. The end of the L-wave marks the point at which all of the injected radiosodium has completed its passage through the left ventricle. Fig. 1 shows a typical normal tracing.

In some cases the curve consists, not of two well-defined waves, but of a single large wave. The reasons why the curves are sometimes monophasic are as yet imperfectly understood and are being investigated.

Precordial tracings show definite deviations in cardiac enlargement, with or without failure, and to date almost have been monophasic. The tracings taken in subjects with enlarged hearts and failure do not appear to differ materially from those in cardiac enlargement without failure. This observation arouses interesting speculations concerning the role of the heart in failure and is being further investigated. Fig. 2 shows curves from two patients with cardiac enlargement, one of whom had clinical signs of failure.

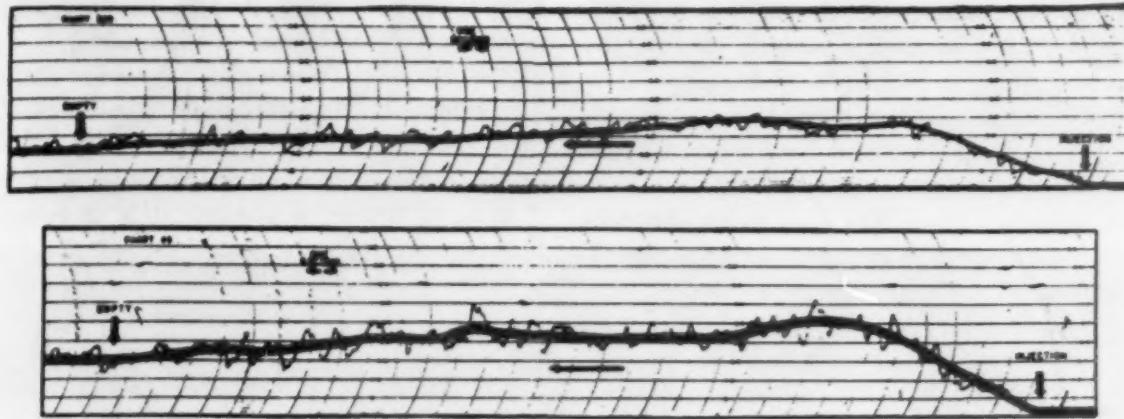


FIG. 2. Radiocardiograms of two patients with rheumatic heart disease, mitral and aortic valvulitis. The upper tracing is of a patient in profound heart failure; the lower of a clinically well patient with a large, dilated heart. Note the prolonged monophasic curves due to the fusing of the right and left waves and the long period of ejection of labeled blood from the left ventricle.

Other observations have emerged from these studies. The rate of venous return from a lower limb is much lower than that from an upper extremity. The slower rate of venous blood flow from the lower limbs, even under normal conditions, helps to explain why there is a far greater tendency for venous thrombosis to develop in the lower rather than the upper extremities.

The recording Geiger-Müller counter has also been used to estimate the time required for a substance to be absorbed from the site of local injection. For example, in one experiment, 0.01 me of radiosodium in isotonic salt solution was injected intramuscularly and a tracing made with the tube placed over the site of injection. In this experiment the results showed that half the injected radiosodium was absorbed in 30 min and almost 90% in 1 hr. Thus, the time required for absorption was much longer than would be anticipated on the basis of commonly accepted clinical impressions. Since we have com-

pleted this phase of the experiment, it has been called to our attention that Kety (1) first utilized this method for the study of absorption.

In controlled experiments on hemorrhagic shock in dogs, it was found that absorption is greatly prolonged during the hypotensive phase. In one experiment, the absorption of radiosodium was 29% in $\frac{1}{2}$ hr while the blood pressure was normal. The mean blood pressure was then reduced to 50 mm Hg. When the experiment was repeated on the opposite limb, it was found that in 30

min only 3% of the sodium was absorbed. After transfusion and elevation of the blood pressure, the absorption returned to normal. In view of the widespread occurrence of shock-like states requiring hypodermic medication, clinical applications of this observation are obvious.

Preliminary observations on congenital heart disease are of interest. For example, in tetralogy of Fallot, the R-wave is normal, but the L-wave is short or absent due to the shunting of blood from the right heart to the systemic circulation.

Radiocardiography has also aided in revealing certain sources of error in the usual clinical methods of determining circulation time and provides a more accurate method of determination.

Reference

1. KETY, SEYMOUR S. *Amer. J. med. Sci.*, 1948, **215**, 352.



Book Reviews

Principles of jet propulsion and gas turbines. M. J. Zucrow. New York: John Wiley; London: Chapman & Hall, 1948. Pp. xiv + 563. (Illustrated.) \$6.50.

This lucid and useful volume contains 61 pages of introductory review of fundamental principles relating to fluid momentum and energy, 86 pages treating gas-flow thermodynamics, 67 pages on airplane and propeller performance, 102 pages on gas turbines and turbojet engines, 93 pages on compressors and turbines, and 70 pages on rocket motors. There are also short chapters on the combustion chamber and high-temperature metallurgy and a chapter of data on the properties of air. There is almost no discussion of the ramjet, the pulse jet, or the solid propellant type of rocket motor.

The treatment of the subject is from the engineering point of view and is in detailed, almost handbook, style. Numerical examples are frequent, and algebraic relations are often supplemented by tables and graphs. The bibliographies at the end of each chapter are quite extensive and, in fact, tend to repeat themselves from one chapter to the next. The effect of the considerable documentation with numerous algebraic steps, tables, and curves might at times be a little confusing to a student in search of a discussion of physical principles.

This book is the first thoroughly quantitative treatment of its subject to appear in the United States since World War II and should fill a definite need for a reference book and undergraduate teaching text, particularly when supplemented with exercises and problems for the student. Some of the review of elementary material available elsewhere may seem repetitious to workers in jet propulsion, but this material will, on the other hand, increase the convenience and value of the book as a source volume for students. The author is to be commended on his thorough and painstaking exposition of an almost encyclopedic body of information.

HOWARD S. SEIFERT

*Jet Propulsion Laboratory,
California Institute of Technology*

Advances in military medicine. (Science in World War II: Office of Scientific Research and Development.) (2 vols.) C. Andrus, et al. (Eds.) Boston: Atlantic-Little, Brown, 1948. Vol. I: Pp. liv + 472; Vol. II: Pp. xvii + 473-900. (Illustrated.) \$12.50 for set.

This two-volume history of the work of the Committee on Medical Research of the Office of Scientific Research and Development provides a massive testimonial to the fact that out of the destruction of war can come medical and scientific advances of value to all mankind.

More than 60 authors, under a distinguished board of editors, all of whom were major contributors to the ad-

vances here described, have written the 54 chapters comprising this record of achievement. The editors include such well-known luminaries as E. C. Andrus, D. Bronk, G. A. Carden, Jr., M. C. Winternitz, J. S. Woodward, J. T. Wearn, and C. S. Keefer. Contributing authors of the chapters themselves, they have done a skillful job of organizing a heterogeneous collection of essays by many authors into a most impressive and unified record of wartime progress in medical research.

It is, of course, impossible in a short space to do more than briefly indicate something of the contents of this publication, one of the more important of the OSRD histories issued under the general title "Science in World War II."

Volume I opens with a foreword by Dr. Alfred E. Richards outlining the organizational history of the OSRD, of which he was chairman. Then follow sections on Medicine, Surgery, Aviation Medicine, and Physiology. Each of the sections is further subdivided into chapters wherein are treated such subjects as Infectious Diseases, Tropical Diseases, Medical Problems of Convalescence, Experimental Wound Healing, The Burn Problem, The Repair of Peripheral Nerve Lesions, The Effects of Acceleration, Anoxia and Oxygen Equipment, Shock, The History of Plasma Fractionation, and Methods of Preservation of Whole Blood.

Volume II includes a series of reports on more specialized problems such as protective clothing, chemical warfare agents, adrenocortical steroids, and sensory devices. Here the reader will also find accounts of such well-known subjects as the development of penicillin, the antimalarial program, and the introduction of DDT.

The almost bewildering variety and complexity of the problems discussed in this work are merely a reflection of the medical, surgical, psychological, and sanitary problems involved in fighting a global war from the arctic to the tropics, in jungles and deserts, under the sea, and in the clouds.

All those who were associated with the work of the Committee on Medical Research will certainly wish to own this record, and all medical scientists will find these books much food for thought, not merely on the problems which still remain to be solved but on methods which may lead to their solution.

Finally, attention is called to a most elaborate and valuable bibliography of those OSRD reports which have already appeared in scientific and medical journals. In addition, there is a list of OSRD Medical Research Contracts sponsored by the Committee on Medical Research. This is arranged by subject in tabular form, including the contract number, the contractor, and the investigator.

MORRIS C. LEIBER

Library of Congress, Washington, D. C.

SCIENCE, September 24, 1948, Vol. 108, No. 2813